



Are electronic cigarettes a healthier alternative to conventional tobacco smoking?

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Abstract

Electronic cigarettes (EC) with and without nicotine are used by more and more consumers within the last decade. The long-term risks of vapor inhalation are unknown. This study should describe the state of the art of knowledge with respect to the following four items: (1) ingredients of the vapor and their potential risks, the influence of EC on smoking of combustible tobacco to (2) adults and (3) the youth, and (4) the side effects of passive vaping. The vapor of EC contains, in comparison to tobacco smoke, less harmful substances, qualitatively and quantitatively. But, due to failing standardization of EC, this comparison is difficult. Adults are often using both, EC and combustible cigarettes dually. In addition, EC were used for supporting smoke-quitting. Unfortunately, consuming EC with and without nicotine due later to a higher risk of conventional tobacco smoking for the user. In general, the effects of passive vaping are unknown. Although the vapor of EC is less harmful than tobacco smoke, EC are not hazard-free lifestyle products. Technical standardization should be desirable. Adult smoker's benefit using EC is given by completely change to EC only. The rates of success using EC for smoke quitting are not well evaluated. Children and their parents should be informed on the risks of EC use as a precursor of combustible smoking mandatorily. Internet selling EC to any non-adult should be forbidden by law. EC ought not to be allowed to weaken non-smoker's rights, and third persons should be protected by the potential hazards of EC vaping.

Keywords Electronic nicotine delivery systems · e-Cigarette · Risks · Head and neck cancer · Ingredients · Gateway hypothesis · Smoking · Smoking cessation · Review

Abbreviations

EC	Electronic cigarette, e-cigarette
ENDS	Electronic nicotine delivery system
ENNDS	Electronic non-nicotine delivery system
PVs	Personal vaporizers
HNB	Heat not burn products
G	Glycerine
PG	Propylene glycol
NNN	<i>N</i> -Nitrosornicotine

Introduction

The history of conventional tobacco smoking in Europe goes back to Christopher Columbus, who came into contact with the tobacco plant for the first time in 1492. He and his companions then brought it to Europe [1]. It spread particularly among the envoy of the French King to the Portuguese court, Jean Nicot (1530–1604), who recommended the tobacco plant as a wonder herb to treat all possible diseases [2]. As a result of this, the plant and its cultivation spread initially in France and then later in Central Europe thanks to the Huguenots [3]. Frederick I of Prussia, father of the soldier king and grandfather of Frederick the Great, recommended tobacco smoke as an antidote to “bad air” [4]. Towards the end of the nineteenth century, the industrial manufacture of cigarettes enabled wide social classes to be supplied with cheap smoking products. The product fit perfectly with the new, fast-moving era, as it could be consumed in just a few minutes during a break on the assembly line or in the trenches [5].

The harmful consequences of tobacco smoking and the addictive effect of nicotine were not known for a long time.

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Initially, many other possibilities such as industrial waste and automobile exhaust gases and the possible late effects of the use of chemical weapons during the First World War were discussed as possible causes of the rapid increase in lung cancer at the start of the twentieth century [6]. Even as late as 1918, the French architect LeCorbusier was still trying to protect himself from being infected with Spanish flu in Paris by smoking large quantities of cigarettes (and consuming cognac) [7]. Fritz Lickint set out the link between the development of bronchial cancer and tobacco smoking for the first time in a study in 1929 [8]. In 1940, Franz Hermann Müller expanded on these investigations with an epidemiological study and coined scientific terms such as “smoke pathway” and “passive smoking” [6]. Like all other areas, research on smoking was ideologically shaped in Germany under the National Socialists. Smoking was deemed to be “un-Aryan”, and the state attempted to suppress it as far as possible [9]. After the end of the Second World War, cigarettes initially functioned as a means of exchange in Germany and were later an expression of the American way of life [10].

In 1950, Doll and Hill were definitively able to show that smoking causes lung cancer [11]. In 1964, the Terry Report summarized the results of more than 7000 studies looking at the harmful effects of smoking [12]. As a result, the link between smoking cigarettes and lung cancer and other diseases became known to the broader medical profession. In the meantime, tobacco smoking has also been linked to or blamed for the development of a large number of diseases [13]. Doll et al. carried out a retrospective investigation of over 34,000 British doctors showing that tobacco smoking reduces life expectancy by an average of 10 years and that statistically each cigarette shortens life by 15 min [14] and exposing the fact that half if not two-thirds of all smokers will die prematurely from the consequences of smoking.

The history of the e-cigarette

Joseph Robinson developed an Electric Vaporizer for medical purposes for the first time in 1927 [15]. In 1963, Herbert Gilbert was granted a patent for an electronically operated cigarette that essentially corresponded to the model commonly used today [16]. However, the product did not manage to become established on the market. This was both due to a lack of high-performance batteries and because the market at the time was not yet ready for this new development, as tobacco smoking in society was generally accepted and the harmful consequences were concealed for many decades after this, in particular as a result of lobby work by the tobacco industry. In 1988, Reynolds developed the “Premier” tobacco heater, but this was also unable to establish itself on the market [17].

In 2003, the Chinese pharmacist Hon Lik developed the electronic cigarette that is commonly used today (e-cigarette, EC). His father had died of the consequences of lung cancer and he was looking for a healthier alternative to satisfy his own craving for nicotine after using nicotine patches and sprays without success. Just a year later, in 2004, the product he developed was marketed in China as a replacement for smoking cigarettes, and in 2006 it was introduced around the world [17]. In 2012, the tobacco took an interest in the technology so as not to miss the “Kodak moment” (in which a new technology threatens to replace an existing technology); Imperial Brands bought the patent from Hon Lik for the equivalent of EUR 55 million [18]. In 2014, liquids containing nicotine used for e-cigarettes were subject to regulation for the first time in the EU Tobacco Regulation [19]. This Directive was transposed into German law in 2016 [20].

Structure of an e-cigarette

One or two battery-powered heating wires evaporate flavored liquid, which sometimes contains nicotine, in an evaporator. The carrier substance is normally glycerin (G) or propylene glycol (PG). The smoke that is generated is then inhaled by the consumer. Since the products are not combustion products, the term “electronic vapor products” is also used, and as a result users sometimes call themselves vapers instead of smokers [21]. As well, EC are also known as e-cigs, electronic nicotine delivery systems (ENDS) or electronic non-nicotine delivery systems (ENNDS), personal vaporizers, or PVs. Distinction is now made between four different generations of e-cigarettes. The first is a disposable product similar to a cigarette, the second has rechargeable batteries. The third has refillable or replaceable tanks and the fourth has a mechanism for regulating the electricity supply to the heating wires and therefore the heating temperature. This ability to control the temperature affects the quantity of vapor generated. All forms continue to be used. In addition to e-cigarettes, there are also e-shishas, and nowadays it is very difficult to tell the difference between them. The original structural differences (e.g. a somewhat more Oriental impression to the e-shishas) have been ironed out to an increasing extent in the meantime, and new designs have been developed that no longer have anything to do with the original products. The new technology encourages people to experiment, and instructions for building your own e-cigarettes with severe 100 W of power and recipe to create your own liquids are easily available online [17, 21]. Liquids which contain cannabis (cannavaping) and other illegal drugs are also consumed using electronic vapor generators (drug vaping) [22].

Heat not burn (HNB) products must be differentiated from e-cigarettes, as in these products it is tobacco and not liquid that is heated. These devices were essentially

developed by competing tobacco companies to avoid patent disputes [23].

A comparison of market share, health economics aspects and consumption behavior

In Germany, around 121,000 people die each year from the consequences of tobacco smoking [13]. The net economic costs, in other words the additional costs caused by the increased morbidity, the associated loss of earnings and contributions to pension schemes as a result of a statistically premature death less the savings in pension schemes as a result of the lower life expectancy, are around EUR 79 billion a year in Germany (in 2015 [24]). In contrast, the tobacco industry's revenue is EUR 20.5 billion each year (in 2016, [25]), income from tobacco tax is EUR 14.2 billion (in 2016 [26]) and income in the advertising industry is EUR 15 million (in 2016 [27]). From an economic and health economic perspective, tobacco smoking is therefore a loss-making activity, with society subsidizing the tobacco industry, state and advertising industry. Germany is now the only EU country in which the EU resolution on a general ban on the advertising of tobacco products has yet to be implemented. A draft law on this by the private office of the Grand Coalition published during the most recent legislative period failed as a result of resistance from the CDU/CSU faction in the German parliament under their former leader Wolfgang Kauder [28].

According to the DEBRA study, around 25% of the adult population of Germany currently smoke [29]; this is the highest value in all Western European countries (for comparison: The Netherlands 19%, United Kingdom 17%, Sweden 7% [29]). The number of children and adolescents who smoke has been declining for years and is currently at a historic low (11/9% [29]). The revenue from e-cigarettes has increased significantly in the past few years. In Germany, it was still only EUR 5 million in 2010, but by 2014 it was already at EUR 400 million [30]. Around 10–14% of adults regularly use e-cigarettes at present [29]. When asked about the reasons for this, 39% state that they want to use a less harmful alternative, 23% want to smoke less as a result of using the e-cigarettes, 15% want to stop smoking with the help of e-cigarettes, 13% use e-cigarettes in non-smoking areas and 10% are protecting the health of those around them [31]. Just 1% of adults consume exclusively e-cigarettes [29, 31]. In contrast to this, more than 50% of 15–18-year-olds have tried e-cigarettes, and the trend is increasing [29]. This pattern has also been observed abroad. Fifty-four percent cite curiosity as their reason for trying them, 44% the attractive flavors and 32% the influence of friends and the internet [32].

Contentious issues in research

Even before the initial introduction of e-cigarettes, a dispute, sometimes to this day a very emotional controversy, ignited that affected both research and the political discussion derived from it. There are two opposing positions: one emphasizing the idea of prevention with a desire to protect the population from a new, avoidable risk by flagging the fundamentally harmful nature of inhaling organic substances, the other seeing the opportunity to get smokers of conventional tobacco products to benefit from the use of e-cigarettes and the associated lower levels of pollution [33].

Issue

In line with a recommendation by the German Cancer Research Centre, the scientific issues set out in this overview of the use of electronic cigarettes and the risks of this, focus on these four points [34]:

1. The ingredients in e-cigarettes and their toxicological (and where applicable carcinogenic) effect,
2. the impact on adult smoking behavior,
3. the impact on adolescent smoking behavior, with the “gateway hypothesis” being discussed in particular, in accordance with which adolescents can be tempted to use conventional tobacco products by the use of e-cigarettes [35], and
4. the effect of e-cigarettes on third parties.

These questions are to be answered using the current literature and recommendations from organizations close to the government. There will then be a clarification of whether and under what conditions e-cigarettes have a positive or a negative effect on the user.

Methods

Shortly after World No Tobacco Day (31 May), on 2 June 2018, internet research was carried out on the topic in the search engines PubMed.gov and google.de using the keywords listed in Table 1. The search time was selected to include current articles in the media published for World No Tobacco Day. The aim of searching with Google was to identify additional sources, particularly those close to the government, books and newspaper/magazine articles that were able to provide relevant information on the topic. All of the publications identified via PubMed and the first hundred results from the hits on Google were evaluated for their relevance to this study using the title or the abstract. To evaluate the question of a possible benefit of e-cigarettes compared to conventional smoking products, particularly cigarettes, it

Table 1 Keywords used in the search engines used and hits Early June 2018 (English translation of German keywords in brackets)

Search engine	Keywords	Hits
PubMed.gov	e-cigarette	2644
	e-cigarette smoking	1806
	e-cigarette toxicity	164
	e-cigarette conventional smoking	239
	e-cigarette gateway	48
Google.de	E-Zigarette (e-cigarette)	6,669,000
	E-Zigarette Alternative (e-cigarette alternative)	377,000
	E-Zigarette Gefahr (e-cigarette hazard)	282,000
	E-Zigarette schädlich (e-cigarette harmful)	136,000

was also necessary to compare the main ingredients of the two products with one another.

Since, on one hand, this area of research is very new and therefore new information arises frequently and, on the other hand, organizations close to the government are only able to make recommendations on the basis of these snapshots of research, it did not seem particularly sensible to prepare a systematic review at this stage. The authors therefore consciously limited their account to a narrative review to provide ENT colleagues with an overview of the current level of knowledge and a recommendation for everyday treatment derived from this.

Results

The number of publications found in PubMed and the hits on Google for each search criterion can be found in Table 1. The comparison of the ingredients in the smoke of conventional cigarettes [36] and the vapor from e-cigarettes can be found in Table 2 [for the bibliography see the table].

Ingredients of e-cigarette vapor compared to conventional cigarette smoke

Carrier substances glycerin and propylene glycol

The main components of the vapor generated by e-cigarettes are glycerin (G) and propylene glycol (PG). The former generates a less irritating, dense, white vapor which is appreciated by hobby vapers who use what are known as high-performance e-cigarettes. However, G leads to a slower flooding with nicotine than PG. The second carrier substance, PG, is also used as theatre and disco smoke and to simulate the development of smoke during fire-fighter and airline staff training. They can also be found in nicotine sprays (e.g. Nicorette®). Irritation of the airways is sometimes observed

with these sprays. Both substances are toxicologically harmless, albeit the consequences of long-term inhalation have not been investigated. The heating in the evaporator causes the initial substances to thermally decompose, in some cases into carbonyl compounds; acrolein is generated from G and formaldehyde and acetaldehyde from PG [37]. All three of these substances are carcinogenic when they are inhaled. The quantities in e-cigarettes vary significantly depending on the product, the electric efficiency and last but not least on the measurement conditions [38]. One problem here is also what is known as dry puffs, in which only a small amount of liquid drips onto the hot wire coil. In contrast to conventional tobacco smoking, carbon monoxide is not generated at all in e-cigarettes [36, 38]. The British Ministry of Health stated that the vapor from e-cigarettes contains a total of 95% fewer harmful substances than conventional tobacco smoke [32].

Tobacco-specific ingredients

The nicotine that can sometimes be found in the liquids is no different from that in conventional tobacco products in terms of its pharmacological effect. It is addictive and has also been blamed for the development of other diseases such as coronary heart disease, type II diabetes and erectile dysfunction [39]. A direct carcinogenic effect is sometimes discussed, but has not been proven [40]. *N*-Nitrosornicotine (NNN) forms even as tobacco leaves dry, and as a DNA adduct has a direct carcinogenic effect. Together with nicotine, it also gets into the liquids when they are manufactured, so it can also be found in the vapor of e-cigarettes which contain nicotine. NNN is also formed endogenously in the bodies of consumers [41, 42]. Like tobacco smoke, the vapor also contains additional alkaloids, nitrosamines and terpenes, some of which come from the tobacco plant and some of which come from the process of thermal decomposition of the liquid [43]. There is a partial pyrolysis of the HNB products, which are not discussed in greater detail here, which in turn leads to another emission spectrum [44].

Flavorings

A total of over 7000 flavorings have been described in the liquids [45]. The majority of these are also used in the food industry, albeit they were only developed for oral consumption. Experience of the long-term effects of inhalation is only available for a few substances [46]. Diacetyl, which is used to create a buttery taste, led to an increased frequency of bronchiolitis obliterans in workers at a popcorn factory [47]. Cinnamon aldehyde, which is used to create a cinnamon taste, is cytotoxic and genotoxic [48]. It also has a high allergenic potential and is part of what is known as the fragrance mix used in allergological diagnostics [48].

Table 2 Comparison between conventional cigarettes and electronic cigarettes (EC)

Cigarettes [36]	EC	References	Toxic effect/notes
Combustion temperature Mainstream 1000 °C Side-stream flow 600 °C	Vaporizing temperature Approx. 250–300 °C no side-stream flow	[36, 37]	Higher temperatures lead to greater decomposition of the organic starting products
Approx. 4800 substances of which > 90 are carcinogenic/DNA-modifying	9–450 times lower concentration of harmful substances 95% fewer harmful substances according to the Ministry of Health GB	[36–38] [32]	Note: The concentration of harmful substances varies significantly depending on the product in EC, and different heating temperatures result in different emissions
Carbon monoxide (CO)	No CO	[36, 37]	Hb block, leads to a reduction in O ₂ and therefore an increase in pulse and blood pressure
Dito Insignificant compared to other ingredients	Propylene glycol	[36, 37]	Irritates the airways (coughing), breaks down into formaldehyde and acetaldehyde (carcinogenic)
Dito Insignificant (see above)	Glycerin	[36, 37]	Lipoid pneumonia possible, breaks down into acrolein (carcinogenic)
Nicotine	Sometimes nicotine	[39, 40]	Addictive coronary heart disease, type II diabetes, erectile dysfunction
NNN	Sometimes NNN	[41, 42]	DNA adduct, see text
Radionuclides (²¹⁰ Po, ²¹⁰ Pb, ²²⁶ Ra, ²²⁸ Ra, ⁴⁰ K, ²²⁸ Th)	No radionuclides	[36, 50]	Only in cigarettes, carcinogenic when inhaled as predominantly α and β emitters Harm: 20 cig./d/a → approx. 8.8 mSv/a
Aliphatic and aromatic compounds	Dito	[36, 37]	Many aromatic compounds are carcinogenic, but the concentration is significantly lower in ECs
Dito Do not play a significant role compared to ECs and the other toxic ingredients	Flavorings (7000 different substances)	[45–50]	Mostly come from the food industry, investigated for oral consumption which is mostly harmless There have been hardly any investigations of the effect of inhalation Decomposition to other substances
Nitrosamines, terpenes	Dito	[36, 37, 41, 43]	Many nitrosamines and terpenes are carcinogenic, but the concentration is significantly lower in ECs
Alkaloids	Sometimes alkaloids	[36, 43]	Predominantly in liquids that contain nicotine
Heavy metals: Cd, Hg, Cu, As, Ni, Zn, Pb, Sb, Au, etc.	Heavy metals: Cd, Ni, Pb etc.	[36, 50]	Cd is carcinogenic and nephrotoxic, inhaled heavy metals can trigger diseases of the airways

GB Great Britain, Hb hemoglobin, NNN N-nitrosornicotine

Cross-allergies with balsam of Peru are common. The substance also reacts with nucleophilic structural components of proteins and can trigger a type IV immune reaction as a result. Benzaldehyde, which is used as a bitter almond and fruit flavor, leads to irritation of the eyes and mucous membranes [49].

Heavy metals

Like tobacco smoke, e-cigarette vapor also contains heavy metals such as cadmium ions and others (see Table 2). Cadmium is nephrotoxic and has a carcinogenic effect.

Inhaled nickel is also carcinogenic and a contact allergen. The origin of the heavy metals has yet to be fully clarified, impurities during the liquid production process are conceivable, as is a release from the hot coils. The heated, metallic hot coils also have a potentially catalytic effect in many chemical reactions. The radionuclides contained in tobacco smoke that are absorbed by the plant from the ground together with phosphate and from the air via the hair structures in the leaves and have a directly harmful effect on lung tissue are not found in e-cigarette vapor (overview in [50]).

Impact on adult smoking behavior

According to the largest and most up-to-date study on smoking behavior among adults in Germany, the DEBRA study, one in ten adults has tried e-cigarettes [29]. Most (71.5%) always or primarily use liquids that contain nicotine. Reasons for consumption were cited as the various tastes, the cheaper price compared to conventional tobacco smoking or the fun factor (> 30% in each case). People stated almost as frequently that they believed e-cigarettes to be less harmful than cigarettes, that they wanted to smoke less or no tobacco, that they wanted to stop smoking or that they wanted to protect those around them from tobacco smoke or to be able to vape in places where smoking is prohibited (around 25–30% in each case) [29]. E-cigarettes are by far the most commonly used method used to support smoking cessation among smokers (9.1%); the success rate was not investigated in the DEBRA study [29].

Impact on children's and adolescent smoking behavior

There are several studies on this, with some of the results varying considerably. According to an investigation carried out with children aged between 12 and 14, 16% of all of those surveyed had tried an e-cigarette, 83% of whom had never smoked [51]. In a study carried out in Frankfurt am Main, 50% of the 15–18-year-olds surveyed stated that they had tried e-cigarettes, and the trend was on the rise [52]. However, only a very small number stated that they vaped every day (2%). E-cigarette users stated more frequently that they also smoked conventional cigarettes, and half of all users use liquids that contain nicotine [52]. There was an increase in the smoking rate following the introduction of the EU Tobacco Directive, which also regulates e-cigarettes that contain nicotine [29, 52]. A cohort study of adolescents aged 15–16 in Lower Saxony and Schleswig–Holstein showed that 14.3% of those surveyed have tried an e-cigarette [53]. During the observation period, 12.3% of the adolescents who had never smoked before started to experiment with conventional cigarettes. The effect was particularly significant in adolescents who were unlikely to start smoking based on their risk profile [53]. This was confirmed by a large study from the US [54].

Effect of e-cigarettes on third parties (passive vaping)

The use of e-cigarettes does not currently come under the Protection of Non-Smokers Act [55]. The exposure of e-cigarettes in the ambient air and therefore the effect on third parties varies by product. As is the case for direct use, there are no studies on the long-term effect of e-cigarettes

on passive consumers. In contrast to conventional tobacco products, there is no what is known as bypass flow, as a result of which the e-cigarette vapor would deviate into the environment when it is not used. The vapor comes exclusively from the user's exhaled mixture and can therefore also not be compared directly with primary vapor [50]. The concentration also depends on the environmental conditions (vaping lounges, festivals, closed rooms, etc.). Existing studies show that the concentration of fine dusts (PM_{2.5} and PM₁₀), nicotine, propylene glycol, glycerin and carbonyl compounds are elevated and the quality of the room air is generally worsened compared to non-polluted room air as a result of the use of e-cigarettes [overview in 50].

Discussion

Electronic cigarettes are often used as an alternative to conventional tobacco smoking, which emits a number of ingredients. Their use also appears to be particularly attractive for adolescents and young adults. As this is a new and mostly voluntary exposure by the population, evidence on the subject is subject to considerable change. Search engine-based research aims to show the current status of scientific discussion.

Quality of studies

Prospective, randomized studies on e-cigarettes are rare. Investigations of smoking and vaping behavior are essentially based on surveys and not on objective measurement values. Unlike with the (albeit particularly high in harmful substances) reference cigarettes (e.g. standard Ky3R4F), there is no standardized e-cigarette, which makes the comparison of different studies more difficult [44]. There is no general legal regulation of e-cigarettes, either as smokable products (with the exception of liquids that contain nicotine), as drugs or as medicinal products. This is, however, urgently required in order to regulate the effects of e-cigarettes on health and the sale of these. Corresponding requirements have been set out for years by the international forum of respiratory societies [56] supplemented by a position paper of the German Society for Pneumology and Respiratory Medicine [57]; these have, however, been largely ignored by politicians with the exception of those in the government responsible for drugs.

The existing studies on e-cigarettes are of varying scientific quality depending on the design. The relatively short period of time for which e-cigarettes have been used means the long-term consequences cannot be estimated. The data on usage behavior are primarily based on surveys and are therefore dependent on the response rate and a possible influence on response behavior by the respondents. At the

same time, statements can be made on the points investigated, albeit with a varying degree of evidence [50].

Ingredients of e-cigarette vapor

Some e-cigarettes contain the same harmful substances as conventional tobacco products (Table 2), even if the concentration of these is generally significantly lower in comparison. There are considerable differences between the products and the various manufacturers, and the emissions also depend on the evaporation temperature and other environmental conditions. This also makes a direct comparison difficult. The German Federal Institute for Risk Assessment has warned of the currently unpredictable long-term consequences of regular exposure to e-cigarette vapor [58]. Reference is made to studies that have shown cytotoxic effects on pulmonary stem cells and pulmonary fibroblasts in vitro, the latter reacting in a significantly less sensitive manner. It is postulated that these effects could have a negative impact on an individual during the growth phase in particular. The cytotoxic effects are considerably less than in comparison with conventional tobacco smoke, but clearly demonstrable [58]. The effects of long-term inhalation of flavorings that were developed for oral use are largely unresolved [50]. Further tests are very much needed on this. Legal standardization of e-cigarettes would make this significantly easier.

Although it is clear that the vapor from e-cigarettes (essentially) contains fewer harmful substances than conventional tobacco smoke and does not contain certain ingredients such as radionuclides and the majority of the carcinogenic substances, the authors feel that it is problematic to estimate the harmful nature of these emissions as a comparison as a flat 95% as the British Ministry of Health has done [32]; this statement is now being used by e-cigarette manufacturers for advertising purposes. As a result, there is a risk of the effect being downplayed in public perception [59]. The risks associated with nicotine consumption also persist [40].

Impact of e-cigarettes on adult smoking behavior

The analysis of the ingredients and further tests have shown that smokers only benefit from e-cigarettes in terms of reducing the harm caused if they switch entirely to these products. As is the case for so-called light cigarettes, the dual use of cigarettes and e-cigarettes results in the pollution levels remaining the same thanks to an increased inhalation depth and frequency of the cigarettes that are still smoked [50, 60]. Explaining this situation to smokers is urgently necessary.

The high acceptance of e-cigarettes by smokers for this purpose compared to evaluated smoking cessation methods [29] offers a certain potential [60]. Previous studies on

this topic have only demonstrated a low level of evidence [60, 61]. Further prospective studies are therefore needed to evaluate the suitability of e-cigarettes as smoking cessation tools. These studies should ideally be randomized and double-blind. The ability to prescribe e-cigarettes which contain nicotine for smoking cessation purposes that the British Ministry of Health [62] is currently trying to implement would leapfrog this necessary step of the acquisition of scientific knowledge.

Impact of e-cigarettes on children's and adolescent smoking behavior

The receptiveness to e-cigarettes, which have only recently become available, among young people is not surprising. The combination of the taste of sweets and the alleged harmlessness, particularly of nicotine-free liquids, appears to mean the psychological barrier to using e-cigarettes is set relatively low, as confirmed by the fact that 50% of all adolescents between 15 and 18 have tried them. The fact that adolescents are being introduced to the use of conventional tobacco products and smoking rituals by the use of e-cigarettes, even those without added nicotine, a fact which has been confirmed by several national and international studies and reviews, is worrying [50, 53, 54, 60]. This would confirm the gateway hypothesis. It is even more concerning that it is not just adolescents who would be at high risk of becoming smokers anyway who are affected, but also those whose individual risk profile (high level of education, high socio-economic class, low degree of personal frustration, low level of risky behavior, etc.) would usually be associated with a low risk of consuming conventional tobacco products, particularly cigarettes. If this trend continues, the rate of smokers among adolescents, which has been decreasing considerably for years, will continue to increase in the future. The only winner from this development would be the tobacco industry.

Educational measures are urgently needed to inform children and their parents of the health risks of e-cigarettes, ideally before they turn to adolescence. The ban on selling e-cigarettes to adolescents under the age of 18 is a first step, but can be circumvented very easily via the internet.

Effect of e-cigarettes on third parties (passive vaping)

There have been hardly any studies on the consequences of passive e-cigarette exposure to date [60]. Although the teratogenic effect of nicotine replacement therapy could not be proven except for the fact that there may be a negative impact on the airways of unborn children [63, 64], no analogous evaluation of e-cigarettes can be derived from these studies. Based on the ingredients, a harmful effect on

children, pregnant women, elderly people and those with a history of cardiopulmonary diseases cannot be ruled out [50, 60]. It is also conceivable that the lack of legal regulation will undermine the hard won protection of non-smokers and that smoking will achieve greater social acceptance again through the consumption of e-cigarettes [54]. Further investigations on this area of topics are also urgently needed.

Conclusion

- Electronic cigarettes generate significantly fewer harmful substances than conventional tobacco products, but their ingredients are by no means harmless.
- Electronic cigarettes are not harmless lifestyle items. The long-term effect of their ingredients is not known, particularly when inhaled; some substances are carcinogenic, e-cigarettes that contain nicotine are addictive and e-cigarettes teach users smoking rituals.
- E-cigarettes can lead to smokers who do not want to or are not able to give up smoking decreasing their exposure to harmful substances, but this can only be achieved if they switch to e-cigarettes completely.
- Electronic cigarettes could be suitable as nicotine replacement therapy to help smokers to stop. There are, however, no reliable data on this.
- Electronic cigarettes hide the risk that use of them could start adolescents on the path to becoming conventional tobacco product smokers (gateway hypothesis); this also applies to nicotine-free e-cigarettes.
- The effect of ECs on third parties is unknown. The ingredients of the vapor, however, are anything but harmless. The risk of the legal protection for non-smokers being softened as a result of e-cigarettes must be countered.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

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