

REVIEW ARTICLE

E-Cigarettes—Prevention, Pulmonary Health, and Addiction

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SUMMARY

Background: E-cigarettes are coming into wider use. They are advertised as an aid to smoking cessation, but there is concern that they may also serve as a gateway drug for cigarette smoking.

Methods: The authors systematically searched the PubMed database for relevant publications on the mechanism of action of e-cigarettes, the nature of their emissions, their assessment by potential users, their efficacy in smoking cessation, and their potential for addiction.

Results: There have been many reports of epidemiologically uninformative case series in which smokers were helped to stop smoking by the use of e-cigarettes. Only two controlled trials have shown that e-cigarettes have approximately the same effect as nicotine substitution therapy when used as an aid to smoking cessation. The effect is nearly independent of nicotine content. E-cigarettes are also consumed, to a small extent, by nonsmokers. As far as can be estimated toxicologically at present, the danger to active and passive smokers of e-cigarettes is presumably orders of magnitude less than that of tobacco smokers, although the variable composition of the fluids used in e-cigarettes introduces a degree of uncertainty.

Conclusion: Preclinical and initial clinical data, including some data from randomized controlled trials, indicate that e-cigarettes may be useful as an aid to smoking cessation or as a means of lowering risk in high-risk groups. In contrast to the demonstrated efficacy of multimodal smoking-cessation programs with pharmacological and psychotherapeutic support, the efficacy of e-cigarettes in smoking cessation has not yet been satisfactorily shown. Valid and informative clinical trials are urgently needed. These should also be designed to determine what predisposition(s), if any, might make the use of e-cigarettes more or less successful than that of other aids to smoking cessation. Moreover, e-cigarettes might be a gateway drug for cigarette smoking; thus, no clear recommendation about their use can be made at present.

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E-cigarettes have been freely on sale since approximately 2008. They were initially sold only online but in the last few years have also been sold in shops specializing in e-cigarettes only. In e-cigarettes, nicotine is “vaped,” i.e. vaporised, instead of being smoked in the conventional manner. There is no scientifically valid data on the use of e-cigarettes in Germany.

According to investment bank Goldman Sachs, the e-cigarette market was one of the eight most important areas of investment in 2013, and the market share of e-cigarettes will rise to 10% by 2020 (*Wall Street Journal*, August 10, 2013). The use of e-cigarettes is expanding very rapidly; on the surface, they suggest the possibility of “healthy smoking.” However, as yet there is no clear scientifically justifiable position regarding e-cigarettes and tobacco cessation (1–3).

Method

This review article involved systematic collation and classification of the available scientific literature on e-cigarettes. The results of the PubMed literature search are shown in the *eBox*.

How e-cigarettes work

An e-cigarette is a battery-operated electronic device that releases aerosolized nicotine for inhalation. No combustion is involved. The terms “e-cigarette,” “electric/electronic cigarette,” “smoke-free cigarette,” and “electronic nicotine delivery device (ENDD)” are more or less used as synonyms. An e-cigarette typically consists of the following parts (*Figure 1*):

- A cartridge in a plastic mouthpiece, containing the liquid to be vaporized
- A heating element that vaporizes the liquid and produces the aerosol for inhalation
- A battery (usually rechargeable) that powers the heating element
- An air flow sensor that activates the heating element and an LED light that produces a glow when triggered by an inhalation.

Contents

The liquid contains varying proportions of the nebulizers or carrier substances propylene glycol (propanediol), glycerin, and water, and sometimes nicotine, pharmacological agents, and various fragrances and

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aromas (e.g. menthol, linalool [“floral”], ethyl acetate [“fruity”], tabanone [“cigarette-like”]). Smokers of e-cigarettes can mix their own liquids, and an almost endless range of substances is available for this; even tadalafil (a male potency enhancer) and rimonabant (an appetite suppressant) have been detected (4). The nicotine content of commercially available cartridges is only loosely correlated with levels declared for them (5), and even with a single liquid the release of aerosols differs significantly between devices (6). As a result, there is no reliable information on the inhaled dose of nicotine available to e-cigarette users. This makes it difficult to provide an unambiguous toxicological risk assessment.

Current knowledge concerning potential and present users

Qualitative focus group interviews with smokers of e-cigarettes revealed five areas which respondents gave as reasons for using e-cigarettes:

- Biofeedback (sensation in the mouth)
- Social benefits (support from others with the same views)
- Hobby (mixing liquids)
- Personal identity (nicotine consumption with no disturbance to others)
- A distinction between smoking and nicotine consumption (7).

In the tobacco control four-country survey, which covered the period from 2010 to 2011 and involved 5939 current and former smokers in Canada, the USA, the UK, and Australia (8), 46.6% of participants were aware of e-cigarettes and 7.6% had tried them. 85.1% of e-cigarette users reported that they used them to stop smoking. E-cigarette users tended to be younger people, those with higher incomes, and heavier smokers.

According to repeat cross-sectional surveys in the UK, the proportion of people aware of e-cigarettes doubled between 2010 and 2012, and the proportion of users increased four-fold (9). The data suggest that awareness and consumption of e-cigarettes will also increase rapidly in Germany; however, no reliable figures on usage are currently available.

Online surveys of 1347 e-cigarette users recruited via manufacturers’ websites indicated that 74% of participants had abstained from tobacco smoking for at least several weeks since using e-cigarettes, and 70% reported reduced cravings (10). The mean length of use in these surveys was 10 months, significantly longer than standard medication-assisted tobacco cessation such as nicotine replacement products.

In a recent cross-sectional study, 320 individuals in Munich were asked why they used e-cigarettes, what they thought about smoking, and whether they intended to stop (Rüther T. et al.: Electronic cigarette [e-cigarettes]—an aid for smoking cessation? Society for Research on Nicotine and Tobacco 2013; International Meeting Boston MA 2013): in those who smoked only e-cigarettes, nicotine dependency as measured using the Fagerström test (11) was signifi-

cantly ($p < 0.05$) lower than in those who smoked conventional cigarettes. In addition, e-cigarette users reported a significantly higher level of confidence that they would be able to stop smoking completely. E-cigarettes were used as an aid to smoking cessation by 50% of individuals. Users also felt healthier than smokers of conventional cigarettes. There were no e-cigarette users who had not previously been regular tobacco consumers (Rüther T. et al.: Electronic cigarette [e-cigarettes]—an aid for smoking cessation? Society for Research on Nicotine and Tobacco 2013; International Meeting Boston MA 2013). However, the literature reveals evidence that people who have never previously smoked do use e-cigarettes: the percentages of Polish (12) and US (13) students were 3.2% and 9.3% of survey participants respectively. It is not yet known how many of these consumers later switch to conventional tobacco products and develop nicotine dependency.

This and many other literature sources, dating mainly from 2012 and 2013, have only the empirical validity of case reports or case series, as they are based on self-selection by study participants and the size of the reference population (i.e. the denominator) is unknown. This means that only the following conclusions can be drawn:

- There are many former tobacco smokers who have weaned themselves off tobacco using e-cigarettes.
- A majority of users consume e-cigarettes for reasons of health.
- In former non-smokers the potential for e-cigarettes to act as a gateway to tobacco consumption, at least in some individuals, cannot currently be ruled out.

Pharmacological action

The nicotine inhaled via this type of e-cigarettes enters the body more slowly than when smoking conventional cigarettes (14, 15) (Table 1). Accordingly, a conventional cigarette suppressed the craving to smoke more than a 16 mg nicotine-containing e-cigarette (15) (Figure 2). There is currently no clinical data available on any direct reward effect, or “kick,” from an e-cigarette.

In an experimental study of 20 tobacco smokers who had abstained from smoking for 8 to 10 hours, it was shown that an e-cigarette containing 18 mg nicotine improved prospective memory when compared to a nicotine-free e-cigarette (16). This demonstrates the acute pharmacological effect on the CNS of nicotine absorbed from an e-cigarette.

Role in tobacco cessation

In addition to nicotine’s direct, short-term reward effect and the long-term dependency-causing psychotropic effect, psychological dependency also plays a significant role in the development and maintenance of a tobacco addiction (ICD-10: F17.2). This psychological dependency involves the following:

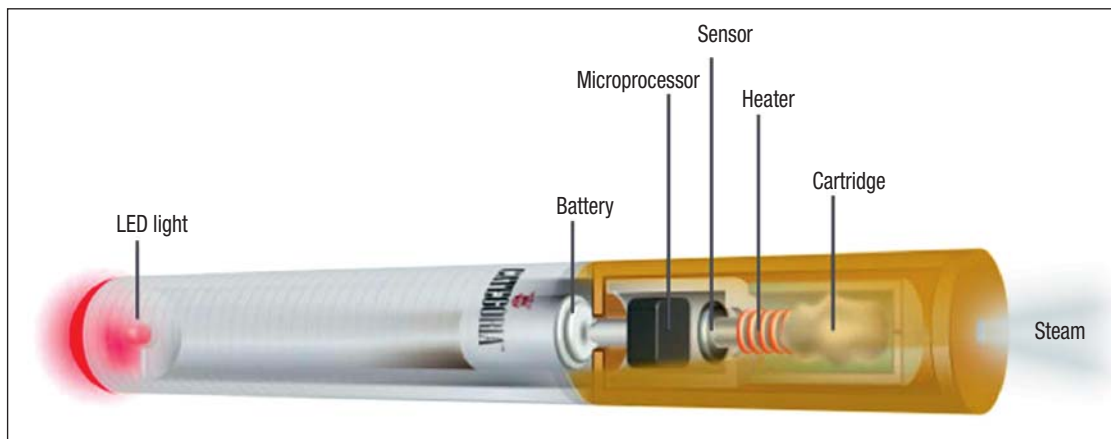


Figure 1: Technical workings of an electronic cigarette (from: Caponnetto P. et al.: Successful smoking cessation with electronic cigarettes in smokers with a documented history of recurring relapses: a case series. *Journal of Medical Case Reports* 2011; 5: 585. Reproduced with the kind permission of BioMed Central)

- Classic conditioning (smoking regularly in particular situations that become themselves triggers for a craving to smoke)
- Operant conditioning (rapid, positive, subjective effects following cigarette smoke inhalation)
- Social reinforcement (membership in a group, development of a “smoker identity”) (3, 17)
- Sensorimotor effects (taste, smell, smoke clouds) of smoking (18).

Initial studies indicate that e-cigarettes can reduce acute cravings almost as much as conventional cigarettes, even at low or undetectable levels of nicotine intake (19, 20). This means they might have the potential to act as a means to wean individuals off the psychological components of smoking.

Because nicotine enters the body very slowly with the current generation of e-cigarettes, at a speed comparable to common nicotine replacement products (14, 15), they may indeed be useful in tobacco cessation programs. Theoretically, this would address the psychological aspects of dependency, including the sensorimotor effects of smoking, and at the same time achieve similar nicotine replacement to common nicotine products. The addiction potential of e-cigarettes themselves in this scenario can be assessed as low.

There are currently only two randomized controlled trials available on the efficacy of e-cigarettes in smoking cessation. The results of a three-arm study (nicotine-containing e-cigarettes/nicotine-free e-cigarettes/nicotine patches with minimal other assistance) with a six-month follow-up period (21) are particularly interesting. Smokers who wanted to stop smoking were recruited by telephone, randomized, and assigned to one of the study arms—nicotine e-cigarette (16 mg), nicotine patch (21 mg), and placebo e-cigarette—at a ratio of 4:4:1.

Members of the e-cigarette groups received the products at home by courier, and the nicotine patch group received coupons that could be redeemed at a

pharmacy for a small fee. Both e-cigarettes and patches were to be used daily from one week before to 12 weeks after a self-determined smoking cessation day.

The six-month continuous abstinence rate, verified via carbon monoxide measurement, was 7.3% (21 out of 289) for the nicotine e-cigarette group, 5.8% (17 out of 295) for the nicotine patch group, and 4.1% (3 out of 73) for the placebo e-cigarette group. With this program, without any additional assistance, the abstinence rates fell below expected levels.

The differences were not statistically significant; this was also true for unwanted or serious adverse effects. The authors concluded that nicotine-containing and nicotine-free e-cigarettes were comparable to nicotine patches in achieving six-month tobacco abstinence. The weaknesses of this study, however, are obvious: no additional assistance or motivation for participants, no placebo nicotine patch study arm, low to no monitoring of compliance, differing availability of smoking cessation aids, no laboratory or other tests.

In another 12-month prospective study (22), smokers who did not want to stop smoking were given e-cigarettes with two different levels of nicotine content. This was a three-arm study; the third arm involved placebo e-cigarettes containing nicotine-free liquids. After one year all three groups showed a statistically significant reduction in daily consumption of conventional cigarettes and levels of carbon monoxide in exhaled air, and there were no significant differences between the groups. Overall, 8.7% of study participants abstained from conventional cigarettes completely. Thus the reduction and abstinence rates in smokers who did not want to stop were comparable to those for nicotine replacement therapy without additional support (23).

Both of the currently available randomized controlled trials on smoking cessation therefore indicate that e-cigarettes can be successful in smoking

TABLE 1

Pharmacokinetics of nicotine in a conventional cigarette, a 16 mg e-cigarette, and a nicotine inhaler (17)

Product	Mean t_{max} (minutes) (95% confidence interval)	Mean C_{max} (ng/mL) (95% confidence interval)
Conventional cigarette	14.3 (8.8 to 19.9)	13.4 (6.5 to 20.3)
16 mg e-cigarette	19.6 (4.9 to 34.2)	1.3 (0.0 to 2.6)
Nicotine inhaler	32.0 (18.7 to 45.3)	2.1 (1.0 to 3.1)

C_{max} : Maximum serum nicotine level
 t_{max} : Time to maximum serum nicotine level C_{max}

reduction and cessation regardless of nicotine content. Further, larger studies of better methodological quality are urgently needed on this subject. It seems advisable to determine whether different treatment conditions for smoking cessation and different patient groups benefit from the available aids in different ways. Because diseases caused by cigarette smoking—such as lung cancer, chronic obstructive pulmonary disease (COPD), and cardiovascular diseases—are so prevalent, all available methods should be tested objectively.

Potential for addiction

For the e-cigarettes currently on the market, the speed with which nicotine enters the CNS after being inhaled is comparable to that of nicotine replacement products (nicotine patches, chewing gums, mouth sprays, or inhalers) and is a matter of minutes. In contrast, when tobacco smoke is inhaled nicotine reaches the CNS within 20 seconds, as a result of tobacco smoke’s more favorable pH for resorption and the binding of nicotine to smoke particles (24). In addition, lower maximum serum nicotine levels have been found following the use of e-cigarettes and therapeutic nicotine products than in smokers of conventional cigarettes (14, 15).

The potential of a drug to cause dependency is strongly correlated with the time between administration and the beginning of central reward effects (25, 26). The addiction potential of nicotine replacement products is therefore extremely low. In this regard, pharmacologically, the low addiction potential of nicotine replacement therapies also holds true for e-cigarettes. To date there is no clear evidence for their hypothetical potential as a drug, particularly among the young. As there is no “kick” from e-cigarettes, as opposed to conventional cigarettes, this risk seems to be low, but it must nevertheless be monitored, especially as it is possible that the cigarette industry might act manipulatively. This is also true for e-cigarettes’ much more worrying but insufficiently researched potential as a gateway drug to cigarette smoking.

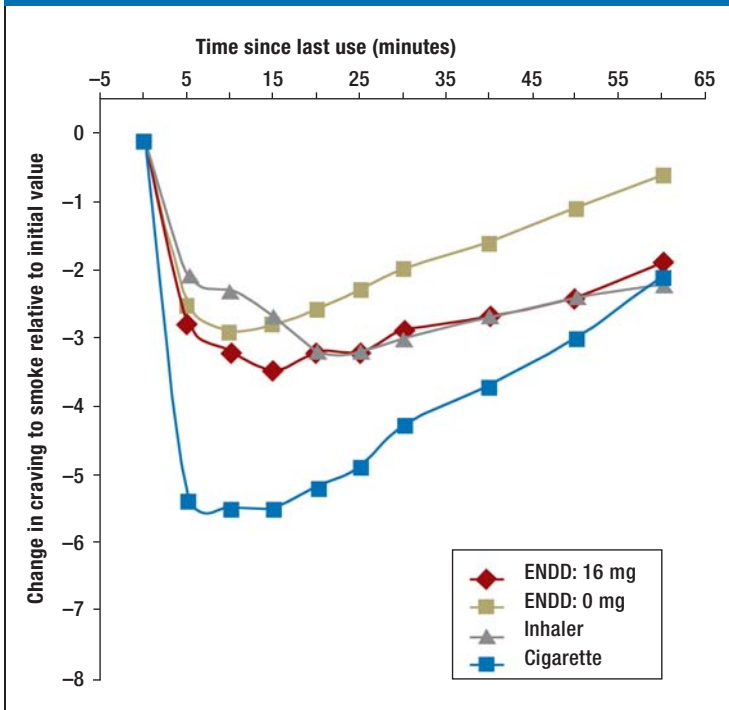
Harm reduction

As yet, there is no data in the available literature on the use of e-cigarettes in high-risk groups such as psychiatric patients. High-risk groups have considerably higher prevalences of smoking than the general population (depression: approximately 60%, schizophrenia: approximately 85%, addictive disorders: up to 95%) (27), they have a significantly higher risk of dying of tobacco-related diseases (28), and they have lower success rates for smoking cessation (29). The use of e-cigarettes for risk reduction is a possible option and should be the subject of future studies.

Pulmonary effects

There is little data available on this subject. In 30 smokers with no manifest airway disease who “vaped” e-cigarettes with an 11 mg nicotine cartridge for five

FIGURE 2



Reduction in craving to smoke following use of various nicotine-containing products—tobacco cigarette (blue), e-cigarette (ENDD: electronic nicotine delivery device) with 16 mg cartridge (red), nicotine inhaler (gray)—versus nicotine-free e-cigarette (0 mg) (olive green); (according to Bullen C, et al.: Effect of an electronic nicotine delivery device [e cigarette] on desire to smoke and withdrawal, user preferences and nicotine delivery: randomized cross-over trial. *Tob Control* 2010;19: 98–103. Reproduced with the kind permission of BMJ Publisher Group Ltd.) (15)

TABLE 2

Harmful substances in conventional cigarette smoke vs. e-cigarette aerosol (36)

Substance	Conventional cigarette (µg in main current of smoke)	E-cigarette (µg in 15 inhalations)	Mean ratio (conventional cigarette vs. e-cigarette)
Formaldehyde	1.6 to 52	0.20 to 5.61	9
Acetaldehyde	52 to 140	0.11 to 1.36	450
Acrolein	2.4 to 62	0.07 to 4.19	15
Toluene	8.3 to 70	0.02 to 0.63	120
N'-nitrosonornicotine	0.005 to 0.19	0.00008 to 0.00043	380
N'-nitrosonornicotine and 4-(methylnitrosoamino)-1-(3-pyridyl)-1-butanone	0.012 to 0.11	0.00011 to 0.00283	40

minutes at will, there was a statistically significant reduction in exhaled nitric oxide (FeNO)—a marker mainly of eosinophilic inflammation—and an increase in respiratory impedances measured via impulse oscillometry (IOS)—an indicator of peripheral airway resistance—when compared to control exposure (no cartridge) (30). Two recent publications (Vakali S. et al.: Short term use of an e-cig: Influence on clinical symptoms, vital signs and CO levels. European Respiratory Society Conference. Barcelona 2013; Palamidis A. et al.: Acute effect of an e-cigarette with and without nicotine on lung function. European Respiratory Society Conference. Barcelona 2013) found on average a significant increase in central airway resistance and an increase in carbon monoxide in exhaled air among both non-smokers and smokers with and without airway disease, regardless of nicotine content of cartridge.

A study by the authors, however, was unable to confirm these FeNO findings (31). In two other studies, no significant effects on conventional lung function parameters or leucocyte populations in the blood were observed when compared to participants who smoked conventional cigarettes (32, 33).

Overall, although the reported acute effects on the airways were slight, from a physiological perspective they must be considered adverse. The fact that small changes in parameters such as FeNO and IOS are susceptible to artefacts, that interpretations are by no means unambiguous, and other factors cause interpretation difficulties. To date there is no data on long-term use that shows clinically relevant target parameters. However, two very recent case reports on potential adverse effects of e-cigarettes are worth further investigation (34, 35).

Toxicological assessment

As e-cigarette use involves no combustion, their emissions would not be expected to contain significant levels of carcinogenic polycyclic aromatic hydrocarbons (PAHs). The fact that they involve a vaporization process also suggests that no significant levels of carbon monoxide are released, so carbon monoxide-

induced cardiocirculatory effects are unlikely. However, in experimental conditions, increased PAH levels have been measured in the surrounding air (31); this finding needs to be verified in various exposure scenarios.

Overall, the levels of harmful substances in e-cigarette vapor are between nine and 450 times less than in conventional tobacco smoke (Table 2) (36). There is no question but that this is a step forward in harm reduction.

The main carrier substance used for nicotine and fragrances is propylene glycol (propanediol). This is a colorless, almost fragrance-free alcohol that is an oily liquid at room temperature. The quantity of propylene glycol at which 50% of experimental animals die (lethal dose 50) is very high in rats (20 g/kg), and its known levels of irritation to the eyes, skin, and airways are low. There is no data yet available on airway-sensitizing effects, reproductive toxicity, genotoxicity, or carcinogenicity; no scientifically justifiable threshold limit value (TLV) has been determined (37).

The carcinogen burden received by people who are exposed to e-cigarette emissions at home, in public spaces (bars, restaurants), or at work is undoubtedly several orders of magnitude smaller than the burden from passive exposure to conventional tobacco smoke (31, 38). This means that, unlike conventional passive smokers, people who are exposed to e-cigarette vapor at home or work are not likely to have a measurably increased risk of lung cancer. Nevertheless, “passive vapor” does contain detectable levels of 1,2-propanediol, 1,2,3-propanetriol, diacetyl, fragrances, and nicotine (39). The burden on those exposed at home or work must therefore be clarified within environmental and occupational medicine as part of the prevention of diseases other than lung cancer (40). A further factor, which is completely independent of toxicology, is the irritation caused to others by the released fragrances.

Outlook

The market share of e-cigarettes will increase. The cigarette industry will enter this market, probably also targeting groups who are not yet consumers—in other words, the young in particular—with cigarettes that are

ostensibly “healthier” because they are smoke-free. This would thwart medical professionals’ efforts to prevent tobacco use among young people. The cigarette industry may try to accelerate nicotine release and increase the quantity of absorbed nicotine in order to attain the “kick” that is well known in cigarette smoke and to support addiction behavior among consumers in the long term. A further aim of the cigarette industry may be to force users to switch to conventional tobacco products later and thereby win back the market share they have been losing. It is impossible to foretell whether such efforts will be successful. In addition, disposable e-cigarettes might cause an electrical waste problem.

Conflict of interest statement

Prof. Nowak has received consultancy fees (Advisory Board) from Pfizer (a manufacturer of smoking cessation aids). He has received lecture fees from GSK. Prof. Nowak is a member of the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area (Senatskommission zur Prüfung gesundheitsschädlicher Arbeitsstoffe) of the German Research Foundation (DFG, Deutsche Forschungsgemeinschaft) and of the Scientific Advisory Board of the German Federal Institute for Risk Assessment (Wissenschaftlicher Beirat des Bundesinstituts für Risikobewertung).

Dr. Jörres has given lectures (on areas of pulmonology unrelated to tobacco cessation) for GSK, AstraZeneca, Boehringer, Novartis, and Mundipharma and has received reimbursement of travel expenses and fees in return. He is a member of the Executive Committee of Germany’s national COPD network, COSYCONET.

Dr. Rütger has received consultancy and lecture fees from Pfizer and Johnson & Johnson. He is a member of the Tobacco Dependency S3 Guideline Committee of the Association of Scientific Medical Societies in Germany (AWMF, Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften). He is a principal investigator of clinical trials on drug-assisted tobacco cessation for the pharmaceutical company Pfizer and Chairman of the German Addiction Medicine Society (DGS, Deutsche Gesellschaft für Suchtmedizin).

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KEY MESSAGES

- The toxicity of e-cigarette vapor is significantly lower than that of conventional tobacco smoke.
- E-cigarettes with and without nicotine have the potential to reduce cravings for conventional cigarettes.
- Nicotine intake via currently available e-cigarettes resembles that of conventional nicotine replacement products more than that of conventional cigarettes.
- E-cigarettes with and without nicotine do in principle have the potential to be a tobacco cessation aid (perhaps primarily in certain subgroups).
- E-cigarettes can have mild acute effects on physiological parameters, but their clinical relevance is doubtful. However, their impact on some sensitive individuals should be clarified.

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REVIEW ARTICLE

E-Cigarettes—Prevention, Pulmonary Health, and Addiction

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eBOX

Literature search

A total of 118 entries in PubMed were identified on January 28, 2014 using the keywords “electronic nicotine delivery device” OR “electronic cigarette” OR “e-cigarette” (English-language only, 2009 onwards). Of these, four were reviews of a general or specific nature, four were studies describing effects in case studies in humans, eight described effects in experimental studies in humans, four described cellular effects, 23 described the composition of e-cigarette liquids and/or vapor (active and/or passive) as well as exposure level and exposure markers in humans, 30 provided data on the use in various populations with or without reference to use as a possible aid for tobacco cessation, three concerned marketing methods, six described use for tobacco cessation in pilot studies or non-RCTs, and four concerned two conducted randomized controlled trials (RCTs) (4, 5). Twenty-eight were commentaries assessing risk-benefit potential and stating a need for research, and four did not address e-cigarettes in any relevant way.

Assessments by the German Cancer Research Centre and the Federal Institute for Risk Assessment

The German Cancer Research Centre (DKFZ, Deutsches Krebsforschungszentrum) indicates the lack of scientific data and rates e-cigarettes as a potential risk due to the high dependency potential of the nicotine they contain. It states that e-cigarettes imitated a watered-down version of genuine tobacco products and that it should be assumed that they made it easier for children and adolescents in particular to take up nicotine consumption. Because e-cigarettes contain nicotine, the DKFZ believes that they should be regulated as drugs (40).

The Federal Institute for Risk Assessment (BfR, Bundesinstitut für Risikobewertung) indicates that because the range of products is large and increasing, the details of what an e-cigarette smoker actually inhales or exhales and what harmful substances are released into the surrounding air are unknown. For consumer protection, it states that e-cigarettes should therefore be treated in the same way as conventional tobacco products in non-smoking areas (www.bfr.bund.de/de/presseinformation/2012/17/e_zigaretten_koennen_auch_zu_gesundheitlichen_gefahren_fuer_passiv_raucher_fuehren-129587.html).

Legal assessment of e-cigarettes as pharmaceuticals

On September 17, 2013 the 13th Instance of Münster Administrative Appeals Tribunal issued three rulings decreeing that nicotine-containing liquids that are vaporized and inhaled using e-cigarettes were not pharmaceuticals; it follows from this that e-cigarettes themselves are not medicinal products.

The first ruling concerned a case brought by a woman whom the health authorities had prohibited from selling nicotine-containing liquids on the grounds that they constituted an unauthorized pharmaceutical. The subject of the second ruling was a press release issued by the state health ministry of North Rhine–Westphalia on December 16, 2011, which warned against selling nicotine-containing liquids because their unauthorized sale was a punishable offence. In the third ruling, two companies that produce and sell nicotine-containing liquids and e-cigarettes filed a suit. They wished to have a court ruling that the liquids were not pharmaceuticals and that the e-cigarettes required to vaporize them were not medicinal products.

The main grounds given by the Administrative Appeals Tribunal in explaining its three rulings were that nicotine-containing liquids were not presented as pharmaceuticals and did not function as pharmaceuticals. According to the standing judiciary authority of the European Court of Justice, decisions on whether products function as pharmaceuticals must be made on a case-by-case basis. According to its statement, pharmaceuticals are typically suitable and used for therapeutic purposes. Nicotine-containing liquids do not meet either of these requirements. The Münster Administrative Appeals Tribunal has authorized review of all three cases (file numbers 13 A 2448/12, 13 A 2541/12, 13 A 1100/12).

On October 8, 2013, as part of tobacco guidelines, the European Parliament passed a draft bill stating that e-cigarettes must be regulated, but not governed by regulations on pharmaceuticals unless they are used to treat or prevent diseases. They must not contain more than 30 mg/mL nicotine, must include health warnings on their packaging, and must only be sold to individuals over the age of 18. Manufacturers and importers must provide competent authorities with a list of all the contents of a product. Finally, e-cigarettes should be subject to the same restrictions on advertising as tobacco products.