Electronic cigarette use in youths: a position statement of the Forum of International Respiratory Societies

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It is the position of @lungsfirst that nicotine in electronic cigarettes poses a great threat to youth and we must protect them from it http://ow.ly/DfWJ30jIes7

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ABSTRACT Children and adolescents are highly susceptible to nicotine addiction, which affects their brain development, even in those who smoke infrequently. Young people who become addicted to nicotine are at greater risk of becoming lifelong tobacco consumers. The use of nicotine-delivering electronic cigarettes has risen dramatically among youths worldwide. In addition to physical dependence, adolescents are susceptible to social and environmental influences to use electronic cigarettes. The product design, flavours, marketing, and perception of safety and acceptability have increased the appeal of electronic cigarettes to young people, thus leading to new generations addicted to nicotine. Moreover, there is growing evidence that electronic cigarettes in children and adolescents serve as a gateway to cigarette smoking. There can be no argument for harm reduction in children. To protect this vulnerable population from electronic cigarettes and other nicotine delivery devices, we recommend that electronic cigarettes be regulated as tobacco products and included in smoke-free policies. Sale of electronic cigarettes should be barred to youths worldwide. Flavouring should be prohibited in electronic cigarettes, and advertising accessible by youths and young adults be banned. Finally, we recommend greater research on the health effects of electronic cigarettes and surveillance of use across different countries.

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Introduction

Smoking is not safe at any age, but prevention in children and adolescents has long been a public health priority. Tobacco dependence starts in childhood; close to 90% of current cigarette smokers start before their 18th birthday. The tobacco industry understands that youths, often referred as "replacement smokers" or "learners" in industry documents, are their critical market [1, 2]. Advertising campaigns have notoriously targeted youths [3–5]. Despite these pressures, teen smoking prevention strategies have generally been successful. For instance, combustible cigarette smoking among middle and high school students in the USA has fallen over the past few decades [6]. Although smoking remains high in some regions of Europe, the Health Behaviour in School-aged Children study showed that weekly tobacco smoking declined among adolescents in almost all countries between 2009 and 2014 [7].

However, a new threat to the health of children and adolescents has emerged, *i.e.* electronic cigarettes or electronic nicotine delivery systems (ENDS), although these devices need not be in the form of a cigarette nor deliver nicotine [8]. They have many other names, including vapes, vape pens, e-hookahs, electronic shishas, mechanical mods, Juul and others, but for the purposes of this position statement, we will use the term electronic cigarettes. Another related method of delivering nicotine, *i.e.* heat-not-burn devices [9], is not discussed here.

Electronic cigarettes deliver aerosols of nicotine and other chemicals to the lung. Although there are no universal or mandatory regulations or standards on content, these devices contain a vehicle (usually propylene glycol and glycerine), flavouring agents and nicotine. Other toxicants can be present as contaminants or generated by heating the solution, and other substances, such as marijuana and cannabis derivatives, can be added to the solution [10, 11]. Additionally, the aerosol exhaled by the user can involuntarily expose bystanders. Most electronic cigarettes release nicotine and other potentially toxic and irritating substances into the air [12].

Following repeated exposure to nicotine, the human central nervous system undergoes structural and functional adaptations, such that the brain requires nicotine to function normally, resulting in complex, biosocial maladaptive behaviours, known as dependence [13, 14]. Given their developmental stage, adolescents and young adults are uniquely susceptible to social and environmental influences to use tobacco [8, 15–17] and nicotine addiction [18, 19]. Several lines of evidence indicate that nicotine exposure during adolescence may have lasting adverse consequences for brain development [3, 20–22], even in those who smoke infrequently. Signs of nicotine dependence can appear within days to weeks of starting occasional use, often before the onset of daily smoking [23]. Data have shown that monthly smoking greatly increases the likelihood of developing dependence in youths [24, 25]. These findings in humans are supported by many animal studies that have provided mechanisms by which nicotine can lead to a pathway of addiction [26].

In 2014, the Forum of International Respiratory Societies, a collaborative of nine international professional organisations that was created to promote respiratory health worldwide, published a position statement concerning electronic cigarettes that outlined existing scientific data and advised caution until more information about their safety and effect on society are known [27]. During the 4 years since its publication, much has been learned about the claimed health benefits and risks of electronic cigarette use, particularly in adolescents and young adults. The current position statement addresses these issues.

Electronic cigarettes and nicotine addiction

With the public's appreciation of the serious health consequences of smoking [28], manufacturers modified tobacco products and marketed them with claims of fewer "toxins" and "carcinogens". These products, such as filtered, "low tar" and "light" cigarettes, have not resulted in less harm [3, 13, 29–31]. Because they are perceived to have lower health risks, electronic cigarettes are the latest addition to the list of industry products implying a beneficial safety profile. Electronic cigarette promoters, users and some professionals judge these electronic nicotine delivery devices to be safer than cigarettes [32–34], despite a lack of strong empirical evidence to support this claim. These judgements miss the point that comparing anything to a product that kills 7 million people each year should have a favourable conclusion and disregard the current trend of decreasing smoking rates without electronic cigarette use.

As noted previously, various nicotine delivery devices are available, with an array of design features and constituent components that significantly influence their pharmacological and toxicological profiles [35]. Evidence is emerging suggesting compensatory behaviours occur in response to this variation, in a manner similar to that identified in cigarettes several decades ago [36]. Electronic cigarettes are as capable of saturating brain nicotinic receptors as conventional cigarettes [37]. This effect may not concur with the nicotine content listed on refill bottles, which may reflect inaccuracy of labelling and manufacturing. Although some studies have shown that nicotine content corresponded to product labelling, analyses of

the ingredients of different flavoured, nicotine and no-nicotine cartridges showed that quality control processes used to manufacture these products can be inconsistent [38]. Some products labelled "nicotine-free" contained nicotine [38]. Electronic cigarettes with higher nicotine concentrations increased subsequent frequency and intensity of conventional smoking and vaping [39]. Also, although self-reported data suggest that 80% of adolescents choose products that do not contain nicotine [40], 99% of electronic cigarettes sold in US convenience stores, supermarkets, drug stores and through mass merchandisers contain nicotine [41].

Pulmonary toxicity of electronic cigarettes

Although the National Academies of Sciences, Engineering and Medicine found substantial evidence that exposure of potentially harmful ingredients from electronic cigarettes is significantly lower than combustible cigarettes [12], it does not mean that electronic cigarette aerosols are "harmless vapour" as industry has claimed in the past [8]. The vapour contains ultrafine particulates, volatile organic compounds and heavy metals, such as nickel, tin and lead [38, 42–44]. The ultrafine particle concentration, size distribution of the particles and deposition pattern in the lungs is similar for electronic cigarette vapour and conventional cigarettes [45, 46]. Electronic cigarettes often come with added flavourants. A flavouring that has been determined to be safe to eat may be toxic when inhaled. These substances are not inert and have been shown to injure airway epithelial cells *in vitro* [47]. Exposure to aerosol extracts causes significant DNA damage in human oral and lung cells, highlighting the need to further investigate the long-term cancer risk of exposure to these products [48]. Inhalation of electronic cigarette aerosols leads to pulmonary inflammation, impaired innate immunity, reduced lung function and changes consistent with chronic obstructive lung disease (emphysema) in pre-clinical animal models [49–52]. Studies in humans, including adolescents, in the USA, South Korea and China have linked their use to chronic or recurrent respiratory symptoms [53–56]. More recently, proteomic analyses of bronchoalveolar lavage collected from nonsmokers, smokers and vapers clearly showed that electronic cigarette vapours exert marked and extensive biological effects on human airways, albeit different than tobacco smoke. These findings suggest that inhalation of vapour is not innocuous and raises concern that electronic cigarettes "should not be prescribed as a safe or harmless tobacco alternative" [57]. Thus, regardless of the presence or absence of nicotine, exposure to electronic cigarette aerosol in adolescence and early adulthood is not risk-free and can result in pulmonary toxicity.

Electronic cigarette use among children and adolescents

Over the past decade, electronic cigarettes have risen rapidly in popularity among young people in many countries [58]. Based on data collected for the US National Youth Tobacco Survey, over 1.6 million high school students and 500 000 middle school students used electronic cigarettes in 2015, 10 times the number of reported users 4 years earlier [59]. An extensive survey of eighth- and ninth-grade students in the state of Oregon found that they were the most common introductory tobacco product used [60]. The product design, flavours, marketing, and perception of safety and acceptability increase the appeal of these products to young people [61]. Electronic cigarette advertisements on internet sites, retail stores, movies and other media are associated with growing use among students. Greater exposure has been associated with higher odds of use [62]. Much of the marketing is through the internet and social networking sites, with posted personal videos displaying the use of the product.

Data on awareness and electronic cigarette use among 35 000 surveyed youths from 25 countries reported overall that their awareness ranged from 15% in Kazakhstan to 80% in Italy and that the past 30-day use ranged from 0.8% in Guyana to 15% among 15-year-old Danish boys and girls [63]. The International Tobacco Control Four-Country Survey, which included data from the USA, Canada, the UK and Australia, found the prevalence of trying electronic cigarettes was higher in young, nondaily smokers because of the perception that they were safer compared with traditional combustible cigarettes [62].

Another common reason for using electronic cigarettes among both youths and young adults is flavouring or taste. Even though flavourings are limited or banned in conventional combustible cigarettes by some countries, they are widely permitted in electronic cigarettes in all nations [64]. These restrictions reflect the well-known use of flavourings to promote tobacco product initiation among adolescents. The lack of regulation creates a fertile environment for the expansion of flavoured electronic cigarette marketing to the young [65]. In 2014, more than 7500 distinct, flavoured electronic cigarette products and solutions were available on the internet with over 250 new products introduced per month [66]. Data from the Population Assessment of Tobacco and Health Study and the National Tobacco Youth Survey revealed that 63–70% of youth users of tobacco products choose flavoured products [67, 68]. Furthermore, data from the National Tobacco Youth Survey showed that flavoured electronic cigarette use was associated with increased risk of smoking combustible cigarettes, supporting a plausible gateway effect [69].

Child and adolescent use of tobacco products reflects experimentation and initiation behaviours that ultimately lead to nicotine addiction. In a large cohort, 81% of youth users of electronic cigarettes reported that their starter product was flavoured compared with 61% and 46% of young and all adults, respectively [67]. Electronic cigarette manufacturers employ diverse and creative strategies to target marketing to adolescents and teens despite widespread bans on the sale of these products to persons less than 18 years of age. Advertising near middle and high schools, in neighbourhoods with high youth traffic, and on television commercials that appeal to youths are common approaches [70–72]. Packaging and display choices, such as candy and fruit iconography on the packaging, displays close to candy, and marketing materials at or below 3 feet (1 m) all enhance interest by youths [73]. For older adolescents and young adults, claimed safety benefits with flavoured electronic cigarettes have encouraged experimentation.

In the USA, electronic cigarette use among students has increased dramatically, and past-30-day use of electronic cigarettes among eighth-,10th- and 12th-grade students exceeded use of conventional cigarettes in 2015 [74, 75]. Among US middle and high school students, both ever and past-30-day electronic cigarette use has more than tripled since 2011. This phenomenon is not restricted to US youth. Although data is lacking for many countries, several national reports have shown marked increases in electronic cigarette use in children and adolescents. Based on survey data, 10–12% of high school students from the UK and South Korea have used electronic cigarettes [76, 77]. According to the National Health Institute survey conducted in Italy, 14% of consumers were adolescents and young adults. Moreover, 24% of Italian adolescent and young adult smokers preferred electronic cigarettes to combustible cigarettes [78, 79]. A large sample of Polish students showed that 24% had tried an electronic cigarette and 7% used them within 30 days of the survey [80]. Similar data have been reported in older Irish teens, with nearly 70% of combustible smokers also using electronic cigarettes [81]. Among students in Finland, aged 12–18 years, 17% had tried electronic cigarettes [82].

Adolescents who use electronic cigarettes tend to be more likely those at higher risk of initiating cigarette smoking [83, 84]. As nicotine addiction develops, the barriers to the use of other tobacco products decrease. Multiple tobacco product use is common among youths.

Nonetheless, there is “substantial” evidence that vaping increases the risk of combustible cigarette use in children and adolescents [85]. While some publications from Great Britain have downplayed the use of electronic cigarettes and their link to combustible cigarette use in adolescents [86, 87], numerous longitudinal studies have confirmed their role as a gateway to more conventional tobacco products [88–91]. A recent large survey of demographically diverse adolescents from 20 schools across England showed that ever-use of electronic cigarettes was strongly associated with smoking initiation and escalation [92]. Meta-analysis of seven studies that included over 8000 adolescents and young adults who were not cigarette smokers at baseline found that among those who had ever used electronic cigarettes, the probability of combustible cigarette smoking initiation was nearly four-fold greater than nonusers [88]. A longitudinal study of US high school students in Connecticut found that electronic cigarette use was associated with subsequent initiation of combustible cigarette use, whereas combustible cigarette use was not associated with subsequent electronic cigarette use. Furthermore, they found that frequency of both electronic cigarette and combustible cigarette use increased over time, consistent with the development of nicotine addiction [93]. The COMPASS study showed that recent electronic cigarette use among Canadian secondary school students was strongly associated with cigarette smoking status and susceptibility to future use [90]. An internet-based survey of young adults in California, aged 18–24 years, found that increased levels of electronic cigarettes use were associated with increased combustible cigarette use: those who used electronic cigarettes regularly smoked combustible cigarettes more heavily than occasional electronic cigarette users [94]. The association between electronic cigarette use and initiation of combustible cigarette smoking was much stronger among adolescents classified as not susceptible to becoming smokers [8]. These data indicate that electronic cigarette use in adolescents does not decrease the likelihood of combustible cigarette use. Rather, “vaping” is associated with increased combustible cigarette smoking among youths.

Youth marketing of electronic cigarettes

Electronic cigarettes are frequently marketed using tactics and themes that have previously been shown to influence use of conventional tobacco products among youths. Exposure of US middle and high school students to electronic cigarette advertising from any source increased between 2014 and 2016, with greatest exposure in retail stores, followed by the internet, television, and newspapers and magazines [95]. However, in contrast to conventional tobacco products, few studies have examined the effectiveness of electronic cigarette advertising and promotions on children and adolescents. A study of 600 British children, aged 11–16 years, showed that electronic cigarette advertising increased the appeal of electronic cigarettes and interest in trying them [96]. In the National Tobacco Youth Survey, exposure to advertising

was associated with current cigarette use among US middle and high school students [62, 97]. Of the 80% of adolescents who were exposed to electronic cigarette advertising in the Youth Tobacco Policy Survey, the great majority said flavourings were a prominent selling feature and that electronic cigarettes were associated with less perceived harm [98]. Indeed, flavourings and harm reduction are common selling points for electronic cigarettes for both internet electronic vendors and retail stores staff [99]. The 2014 US Surgeon General Report concluded that advertising and promotional activities by the tobacco companies cause the onset and continuation of smoking among adolescents and young adults [3], and evidence to date suggests they have the same impact on electronic cigarette use by youths. For this reason, advertising and promotion of electronic cigarettes in media that can be accessed by youths should be banned, and these activities for electronic cigarette manufacturers must be closely monitored.

Regulation of electronic cigarettes

Electronic cigarettes are variably regulated around the world [100]. In 25 countries, their sale is banned. In other nations, they are regulated as tobacco-related products, medicines, poisons, electrical appliances or consumer goods. Even in Europe, electronic cigarette regulation varies widely. Some countries apply many regulatory domains whereas others apply few. For instance, Portugal has regulations on child safety, advertising, promotion, sponsorship, health warning labelling, ingredients, flavours, minimum age, nicotine volumes and concentrations, reporting, safety, sale, tax, and vape-free areas. In contrast, Switzerland has no regulation but prohibits sale of nicotine-containing devices. Norway recently lifted its ban on electronic cigarettes, but Belgium, Austria and Turkey prohibit the sale of all products.

In 2016, only 23 countries had implemented minimum age-of-purchase policies [100], although a law on a minimum age-of-purchase has little or no effect if it is not enforced. Minors are easily able to purchase electronic cigarettes from the internet because of absent or weak age verification measures used by vendors. A recent study showed that minors successfully received deliveries of electronic cigarettes from 77% of purchase attempts and delivery companies never attempted to verify their age at delivery [101].

Data from six European countries indicated that electronic cigarette sales fall with price increases [102]. Another large study from European countries, which included adolescents and young adults, found that the prevalence of electronic cigarette use was proportionate to current conventional cigarette smoking. Large pictorial health warnings on tobacco products were negatively associated with current electronic cigarette use [103].

Strong regulation can protect youths from electronic cigarettes. In 2008, Korea regulated electronic cigarettes as tobacco products with prohibitions on indoor use, sales to minors, advertising bans, health warnings and taxes. While various municipalities have restricted the sale of electronic cigarettes to adolescents and young adults, there had been little federal regulation in the USA. From 2011 to 2015 the prevalence of the use of electronic cigarettes remained stable at about 4% in Korea, whereas it rose dramatically from 1% to 11% in the USA during the same period [104].

In 2016 there was a decline in electronic cigarette use in US middle school and high school students [74], temporally associated with the Food and Drug Administration enacting the “deeming rule” that broadened the definition of “tobacco products” to include electronic cigarettes, and made them subject to regulations set by the Family Smoking Prevention and Tobacco Control Act [65]. Concurrently, use of combustible cigarettes did not significantly change, which contradicts the hypothesis that use of electronic cigarettes protects adolescents from initiation of regular smoking. Increasing awareness of possible negative health effects of electronic cigarette use and control strategies at the national and state levels may have contributed to the reduction in electronic cigarette use in the USA [65]. However, a longer trend is needed to make firm conclusions, and continued vigilance is needed to further reduce electronic and combustible cigarette use among youths.

Conclusion and recommendations

ENDS are devices that deliver aerosols of nicotine and other volatile chemicals to the lung. Their use has rapidly escalated among youths and they are now the most commonly used tobacco product among adolescents. Initiation of electronic cigarette use is strongly associated with the subsequent initiation of combustible tobacco product use among adolescents. Electronic aerosols contain potentially harmful ingredients that often lead to lung injury and chronic respiratory symptoms in users. Hundreds of electronic cigarette brands with thousands of unique flavours are now on the market and some flavourings have been associated with lung toxicity. Indeed, flavourings increase the appeal to youths. Even though it is widely accepted that electronic cigarettes are harmful to youths and lead to nicotine addiction, their regulation varies widely between countries. Existing laws designed to prevent youth access of electronic cigarettes are frequently not enforced.

Based on this information, the Forum of International Respiratory Societies recommends:

1) To protect youths, ENDS should be considered tobacco products and regulated as such, including taxation of electronic cigarettes and supplies. The addictive power of nicotine and its adverse effects in youths should not be underestimated.
2) Considering the susceptibility of the developing brain to nicotine addiction, the sale of electronic cigarettes to adolescents and young adults must be prohibited by all nations, and those bans must be enforced.
3) All forms of promotion must be regulated and advertising of electronic cigarettes in media that are accessible to youths should cease.
4) Because flavourings increase rates of youth initiation, they should be banned in electronic nicotine delivery products.
5) As electronic cigarette vapour exposes nonusers to nicotine and other harmful chemicals, use should be prohibited in indoor locations, public parks, and places where children and youths are present.
6) While their health risks are increasingly recognised, more research is needed to understand the physiological and deleterious effects of electronic cigarettes.
7) Routine surveillance and surveys concerning combustible and electronic cigarette use should be carried out in many settings to better understand the scope and health threat of tobacco products to youths in different countries and regions.

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