Achieving appropriate regulations for electronic cigarettes

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Ther Adv Chronic Dis

2014, Vol. 5(2) 50–61

DOI: 10.1177/2040622314521271

***Abstract*:** A growing body of scientific studies show that e-cigarettes may serve as an acceptable substitute for smoking tobacco cigarettes, thereby reducing or eliminating exposure to harmful elements in smoke. The success of e-cigarettes is such that sales of these products are rapidly gaining on traditional cigarettes. The rapidly evolving phenomenon is raising concerns for the health community, pharmaceutical industry, health regulators and state governments. Obviously, these products need to be adequately regulated, primarily to protect users. Depending on the form and intended scope, certain regulatory decisions may have diverse unintended consequences on public health and may face many different challenges. Ideally, before any regulations are enacted, the regulatory body will require sufficient scientific research to verify that a problem does exist, quantify the problem, explore all potential solutions including making no change at all, determine the possible consequences of each, and then select the solution that is best for public health. Here we present an overview on the existing and deeming regulatory decisions for electronic cigarettes. We challenge them, based on the mounting scientific evidence with the ultimate goal of proposing appropriate recommendations while minimizing potential unintended consequences of ill-informed regulation.

Keywords: cigarette smoking, electronic cigarettes, nicotine use, regulation, regulatory agencies, tobacco harm reduction

Introduction

Cigarette smoking is a deadly and remarkably addictive behaviour. Smoking is such a difficult addiction to break that millions of people smoking today will never be able to quit [Tobacco Advisory Group of the Royal College of Physicians, 2007]. Many smoking cessation medications [i.e. nicotine replacement therapy (NRT), bupropion and varenicline] are accessible to those determined to quit [Polosa and Benowitz, 2011], but they lack high levels of efficacy in real-life settings [Casella *et al*. 2010]. Clearly, a different, more effective approach is needed to reduce the harm from cigarette smoking.

Electronic cigarettes (e-cigarettes or electronic nicotine delivery systems) are battery-operated devices designed to vaporize a liquid solution of propylene glycol or vegetable glycerine which also contains water and flavourings and may or may not contain nicotine. Puffing activates a battery-operated heating element in the atomizer and the liquid in the cartridge is vaporized as a plume of mist that is inhaled. Because e-cigarettes do not burn tobacco, these products are a much lower risk alternative to traditional cigarettes [Caponnetto *et al*. 2012].

In addition to creating vapour which visually resembles smoke, e-cigarettes replace most of the sensory, behavioural and social components associated with smoking. For this reason, they are increasingly used as substitutes for tobacco cigarettes [Caponnetto *et al*. 2013b]. Moreover, internet surveys [Etter, 2010; Siegel *et al*. 2011] and clinical trials [Polosa *et al*. 2011, 2013] show that the e-cigarettes may help smokers quit smoking or reduce harm by smoking fewer tobacco cigarettes, without any remarkable adverse events or risks [Caponnetto *et al*. 2013a], for the user or for the bystander [Burstyn, 2013]. Even compared with NRTs, such as nicotine patches, e-cigarettes prove to be more effective and with a tolerability rate similar, if not better, to that obtained with the

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patches [Bullen *et al.* 2013]. As a consequence, popularity of these products has increased exponentially in developed countries. According to a mail-in survey of more than 10,000 US citizens conducted by the Centers for Disease Control and Prevention (CDC), ever use of e-cigarettes quadrupled to 2.7% from 2009 to 2010 [Regan *et al.* 2013]. Moreover, a follow-up survey from the CDC indicates that e-cigarette use doubled again from 2010 to 2011 [King *et al.* 2013]. The success of e-cigarettes as a tobacco cigarette substitute is such that these products are rapidly gaining on traditional cigarettes [Adelman *et al.* 2013]. Their popularity appears to be related to the fact that they can be used in smoke-free areas, to their competitive price, and to the perceived potential for harm reduction compared with traditional cigarettes [Etter, 2010; Siegel *et al.* 2011].

Obviously, these products need to be adequately regulated, primarily to protect users. But policy makers and regulators must be careful. Depending on the form and intended scope, certain regulatory decisions may have diverse unintended consequences on public health and may face many different challenges.

In this article, we appraise existing regulatory decisions in the light of current scientific evidence and consumer insights with the goal of assisting policy makers identifying and addressing concerns while minimizing potential unintended consequences of ill-informed regulation.

The precautionary principle

Many antitobacco organizations have called for restrictive regulations, pointing out that the health risks have not been studied extensively. The precautionary principle may be invoked when a phenomenon, a product or a process with potentially dangerous effects has not been subjected to full scientific and objective evaluation so that the harm cannot be determined with sufficient certainty. Resorting to the precautionary principle requires the adoption of proportional measures to the level of protection sought. In other words, policies based on the precautionary principle tend to avoid the production of possible risks, not yet scientifically proven. Therefore, they are precautionary and preventive policies [Wiener, 2013; Grandjean, 2004].

This principle has been recognized in international law, especially in environmental matters. A first reference to the precautionary principle is found, in fact, as a general recommendation, in the Final Declaration of the United Nations Conference on Environment held in Stockholm in 1972 [United Nation Environment Programme, 1972]. But the real consecration of the principle in the international field is in the Declaration adopted at the conclusion of the United Nations Conference on Environment and Development (UNCED) held in Rio de Janeiro from 2 to 14 June 1992 [United Nations Conference on Environment and Development, 1992]. From the protection of the environment, the application of the precautionary principle has been extended subsequently to the protection of human and animal health in the food [Convention on Biological Diversity, 2000].

The precautionary principle has also been introduced in EU law by the Treaty of Maastricht, which makes it one of the fundamental principles of Community environmental policy. The Lisbon Treaty confirmed the location of the precautionary principle [European Union, 2008].

Although the first formulations of the precautionary principle were related to the sphere of environmental protection, they were extended to the areas of health, food policy and consumer protection, especially thanks to the intervention of the Court of Justice of the European Union and the Court of First Instance. That court, in fact, in an important decision on the revocation of the marketing authorization of antiobesity drugs [Court of First Instance, 2002, 2003], has stated that, despite being mentioned in the treaties only in relation to environmental policy, the precautionary principle covers a wider application. It is intended to be applied to ensure a high level of health protection, consumer safety and the environment in all areas of Community action. The same interpretation was given by the Court of Justice [Court of Justice, 1998, 1999, 2000].

The Community law laid down the characters of the precautionary principle. The Court of Justice, in fact, in many judgments [Court of Justice, 2010a, 2010b], specified that it is not sufficient that the precautionary measures taken by Member States are objective and respectful of the principles of proportionality and nondiscrimination, but it is also necessary that they are based on the existence of a risk to health endorsed by clear scientific evidence and not purely hypothetical considerations.

First, the Court pointed out that the proper application of the precautionary principle presupposes

the identification of potentially negative consequences for the health arising from the use of a particular product. Second, the precautionary principle requires an overall assessment of the risk to health based on the most reliable scientific data available and the most recent results of international research. If the available data is insufficient or imprecise and doesn't allow to determine with certainty the existence or extent of the risk feared, but there is the likelihood of real harm to public health in which the risk materialize, the precautionary principle justifies the adoption of restrictive measures, provided that they are objective and non-discriminatory.

For these reasons, for example, in the case law Commission *versus* French Republic in 2010 [Court of Justice, 2010a], the Court of Justice has found no grounds for the restrictive measures imposed by France on the placing of foodstuffs additive on the national market from other Member States. In this case, the restrictions were introduced by the French legislature to avoid the potential risks to public health posed by certain categories of admixtures. However, the Court of Justice has found that, even in the presence of risks relating to certain categories of foodstuffs additive, the national legislation must be specific and clearly justified in relation to these categories and cannot be limited to generally exclude the use of all addictive drugs or of foods in which they are employed. The restrictive measures adopted, therefore, were not based on the demonstration of the conditions for the application of the precautionary principle.

In the Community context, especially in light of the considerations contained in the European Commission Communication of 2 February 2000 on the application of the precautionary principle [European Commission, 2000], any burden of proving the danger associated with a product is up to the consumers or to the associations that represent them. In contrast, in the face of a measure taken under the precautionary principle, producers, manufacturers or importers may be required to demonstrate the safety of the product subject to limitations.

In particular, the potential consequences of specific actions to prevent the risk to public health must be assessed. But this would require risk assessments studies necessitating many years to complete. The Network for Public Health Law stated, 'This is precisely when the precautionary principle should be applied' [Subramaniam, 2013]. Moreover, the Science and Environmental Health Network stated, 'The key element of the principle is that it incites us to take anticipatory action in the absence of scientific certainty'. However, the consortium points out that the process of applying the principle must be 'open, informed, and democratic, and must include potentially affected parties. It must also involve an examination of the full range of alternatives, including no action' [Science & Environmental Health Network, 1998].

So far, most regulatory bodies have failed to include the parties most deeply affected by the regulation of e-cigarettes: consumers. Regulators have also failed to examine the full range of alternatives, including taking into account the health risks of maintaining the *status quo*, continued smoking. Rulings of national and international bodies around the world range from no regulation at all to complete bans [WHO, 2009].

The first report by the World Health Organization (WHO) Study Group on Tobacco Product Regulation that addressed e-cigarettes advised a precautionary approach, for the most part, because the evidence about the safety and cessation or harm reduction efficacy of e-cigarettes was virtually nonexistent at that time [WHO, 2009]. The report also stated that more research on e-cigarettes had to be conducted to prove efficacy and safety of these products. Today, a growing body of scientific studies on e-cigarettes and liquids supports the efficacy and safety of these products. Even smokers who do not want to quit may do so when introduced to e-cigarettes [Polosa *et al*. 2011, 2013] and the overall level of risk is much lower than cigarette smoking, with no chemicals raising serious health concerns in e-liquids [Cahn and Siegel, 2011; Goniewicz *et al*. 2013]. In the most comprehensive systematic review of chemical studies to date, Burstyn concluded that there is no evidence that 'vaping', that is neologism, coined to indicate the act of vaporizing the liquid contained in e-cigarettes, produces inhalable exposures to contaminants of aerosol that would warrant health concerns [Burstyn, 2013]. However, chronic inhalation data in humans are needed before any definite conclusions are made.

From a public health perspective it is important to consider the impact of e-cigarette use on bystanders. The existing evidence from

environmental exposure and chemical analyses of vapour indicates that the effects of e-cigarette use on bystanders are minimal compared with conventional cigarettes [McAuley *et al.* 2012; Schripp *et al.* 2013]. This is not surprising considering the nature and levels of contaminants in the vapour and the notion that, unlike tobacco cigarettes, sidestream smoke exposure is nonexistent in e-cigarettes, that is, the only vapour released into the air is that exhaled by the user, not by the e-cigarette itself.

Regulatory authorities have expressed concern about e-cigarette use by youngsters or by never smokers, with e-cigarettes becoming a gateway to smoking or becoming a new form of addiction. However, such concerns are unsubstantiated by existing data that e-cigarette use by youngsters is virtually nonexistent unless they are smokers [Centers for Disease Control and Prevention, 2013; Dockrell *et al.* 2013; Camengaa *et al.* 2014] and in fact the use of e-cigarettes may serve as a gateway 'out' of smoking [Polosa and Caponnetto, 2013a].

In Canada, electronic products that dispense nicotine by inhalation fall under the Food and Drugs Act of Health Canada and thus cannot be imported, marketed or sold in Canada without being approved as a new drug. Likewise, the delivery system of an e-cigarette containing nicotine must meet the requirements of the Medical Devices Regulations. This ruling has resulted in a regulatory grey zone whereby e-cigarette cartridges and liquids that contain nicotine are illegal and cartridges and liquids without nicotine (and with no accompanying health claim) are legal. This irrational situation is contributing to the paradox that many Canadian smokers have to break the law to use an e-cigarette that helps them to refrain from smoking.

If e-cigarettes were being marketed to the general public as a new gadget that every man, woman and child should try, it would make sense to slow down product development and severely limit distribution. But the intended use of e-cigarettes is to serve as a substitute for the practice of smoking tobacco cigarettes. Therefore, it is a product marketed for and to smokers; and inhibiting the distribution serves to harm public health by perpetuating exposure to substances in smoke that cause serious diseases and early death.

Long-term nicotine use and smoking abstinence

The harm of tobacco smoking to the individual and to the society is well known. It is the single most important cause of avoidable premature mortality in the world, killing nearly 6 million people a year [WHO, 2008; US Department of Health and Human Services, 1990]. The WHO Framework Convention on Tobacco Control advises that the key to reducing the health burden of tobacco is to encourage abstinence among smokers [WHO, 2003]. In fact, all medically approved treatments for smoking, whether pharmaceutical or behavioural, have focused on total abstinence from nicotine. That approach would make sense if nicotine caused smoking-related diseases. However, nearly all the health risks come from tar, chemicals and other substances found in the smoke, not from nicotine [US Department of Health and Human Services, 2010]. Products that deliver nicotine without the smoke carry no more than 1% of the health risks of smoking [Phillips *et al.* 2006]. Decades of research on Swedish smokers who switched to snus (a type of moist snuff) showed no increased risk of any type of cancer, cardiovascular disease or lung disease [Lee, 2011]. Similarly, a review of 120 studies on NRT products found that NRT is associated with adverse effects that may be discomforting for the patient but are not life threatening [Mills *et al.* 2010].

If the nicotine abstinence approach was working to rapidly reduce the number of smokers, it might make sense to continue insisting. But this is not the case. Using simulation models, Levy and colleagues predicted that even if the current number of quit attempts in the USA instantly doubled and the number of smokers using pharmacotherapy instantly doubled as well (and these changes were sustained over time), the nation could not reach its goal of lowering adult smoking prevalence to below 12% by 2020 unless the effectiveness of pharmacotherapy increased as well [Levy *et al.* 2010]. A doubling in treatment effectiveness alone would lower smoking prevalence in 2020 from a predicted 17.5% to 15.9%. We all agree that complete smoking cessation is the best outcome for smokers, but for those who experience very long-term, perhaps lifelong, disruption of brain function, mood or cognitive ability following smoking cessation, nicotine cessation may not be the healthiest approach. Such individuals may require long-term treatment support or nicotine maintenance to enable them to maintain smoking abstinence [Tobacco Advisory

Group of the Royal College of Physicians, 2007; Piasecki *et al*. 1998; Caponnetto *et al*. 2013c]. Consequently, many smokers will keep smoking because when given only the options of smoking or completely giving up nicotine many will not give it up. Bearing in mind that nicotine *per se* does not cause much risk when separated from inhaling smoke, it is important to consider that a third option is also available to smokers; the reduction of smoking-related diseases by taking nicotine in a low-risk form. Tobacco harm reduction (THR), the substitution of low-risk nicotine products for cigarette smoking, is likely to offer huge public health benefits 'by fundamentally changing the forecast of a billion cigarette-caused deaths this century' [Sweanor *et al*. 2007].

Several smoke-free nicotine products have been proposed for THR, including NRTs, snus, and dissolvable tobacco orbs, strips, and sticks. Realistic alternatives need to be as readily available as cigarettes, competitively priced, socially acceptable, and approved for regular long-term recreational use rather than as short-term cessation aids. In the UK, NRT products have been recently licensed for longer term use, as well as other harm reduction purposes [Beard *et al.* 2013]. Likewise, in April 2013, the United States Food and Drug Administration (FDA) announced changes in labelling of NRT products that would eliminate warnings against smoking while using NRT or using multiple NRT products. The directions to stop using the NRT after a specified number of weeks will be replaced with a statement that encourages use as long as needed to prevent relapse [FDA, 2013a]. Because of their similarities to smoking, including the hand-to-mouth repetitive motion and the visual cue of a smoke-like vapour [Caponnetto *et al*. 2012, 2013b], e-cigarettes are proving to be an attractive and popular long-term alternative to tobacco cigarettes. The entry of several major tobacco companies into the e-cigarette market, either by acquisition or new product introduction, is another clear indicator of product popularity [Coghlan, 2013; Esterl, 2012]. Hopefully, the e-cigarette business will accelerate transformation of tobacco corporations into becoming nicotine companies, which would be a corporate and public health win.

E-cigarette regulation and associated challenges

The rapidly evolving phenomenon of the e-cigarette is raising concerns for those in the health community, for those in the pharmaceutical industry, health regulators and state governments [The C.S. Mott Children's Hospital, 2013; Sullum, 2013; Knight, 2013; Tierney, 2011]. Among their concerns, there is the fact that e-cigarette use may encourage higher consumption of nicotine, may perpetuate smokers' addiction to nicotine making them less susceptible to quitting altogether, may expose users to the risk of accidental ingestion of e-liquid or as yet unknown health risks from long-term e-cigarette use, may make smoking socially acceptable again thus undermining current no-smoking policies, and may act as a gateway to tobacco, especially for youngsters. Although these concerns are mostly theoretical and not based on scientific evidence, international agencies and regulatory authorities in many countries are investigating or planning to introduce restrictions on the quality, marketing, sale and use of e-cigarettes.

Addressing these diverse concerns may be difficult. The challenge faced by regulators is determining which interventions will have the greatest beneficial impact on public health [Freiberg, 2012]. Addressing one concern without gathering sufficient data or considering other viewpoints often results in unintended consequences. For example, the draft EU Tobacco Products Directive (TPD) circulating late in 2012 called for a limit on nicotine content of no more than 4 mg per ml of liquid [European Commission, 2012]. EU regulators may have believed that 1 ml of liquid is equivalent to one cigarette. However, 1 ml of liquid delivers as many puffs of vapour as the puffs of smoke from an entire pack of cigarettes. Certainly they would not expect a pack-a-day smoker to meet his or her daily nicotine needs with the equivalent of one piece of nicotine gum.

In the first half of 2013, EU health ministers tried to move towards a more restrictive change to the text of the TPD in that all e-cigarettes would have been subject to pharmaceutical regulation regardless of their nicotine content. But during the first reading of the TPD, on 8 October 2013, there was a successful turnaround: e-cigarettes should be regulated, but not be subject to the same rules as medicinal products unless they are presented as having curative or preventive properties. Those for which no such claims are made should contain no more than 30 mg/ml of nicotine, should carry health warnings and should not be sold to anyone under 18 years old. Manufacturers and importers would also have to supply the competent

authorities with a list of all the ingredients that they contain. Finally, e-cigarettes would be subject to the same advertising restrictions as tobacco products [European Parliament, 2013].

Classifying them as medical products in the EU would have meant they would undergo a costly and lengthy authorization process before marketing. As a consequence, product prices would increase, possibly to the point at which switching to a low-risk e-cigarette would be much more expensive than continued smoking. Access to e-cigarettes would be hindered not only because they would only be purchased in accredited pharmacies, but also because their internet sales would be strictly regulated. In these authors' opinion, it is counterproductive and hypocritical to over regulate a product designed to reduce or eliminate the diseases and early deaths caused by smoking. The above-mentioned points have been extensively debated in recent commentaries [Hajek *et al.* 2013; Cobb and Cobb, 2013; Polosa and Caponnetto, 2013b].

However, the unintended consequences of regulating e-cigarettes as medical products have been ignored by the Medicines and Healthcare Products Regulatory Agency (MHRA). In June 2013, MHRA announced UK government backing on medicinal regulation of e-cigarettes and other nicotine containing products in the belief that this is the only way to ensure high-quality products, correct monitoring of the risks and proper control of advertising [Medicines and Healthcare Products Regulatory Agency, 2013].

Of note, the above-mentioned issues may not apply when considering countries with a very low smoking prevalence. Let us take the example of Australia. The Australian Government believes it is not worth the risk of introducing e-cigarettes because they are already gaining substantial success in reducing smoking prevalence with their current antismoking laws [Department of Health and Ageing, 2011]. Thus the decision of the Australian Therapeutic Goods Administration to ban ciga-like e-cigarettes, that is e-cigarettes resembling in shape conventional tobacco cigarettes, is understandable [Therapeutic Goods Administration, 2013]. However, it must be appreciated that Australia is the first nation to sponsor a government-funded trial aimed to test the viability of e-cigarettes as a safer, permanent replacement for tobacco [Duff, 2013].

The FDA first attempted to regulate e-cigarettes under the Food, Drug, and Cosmetics Act as a 'combination drug-device product that requires pre-approval, registration, and listing with the FDA' [US District Court for the District of Columbia, 2010]. The US Court of Appeals for the DC Circuit, in Sottera, Inc. *versus* Food & Drug Administration, 627 F.3d 891 (D.C. Cir. 2010), held that e-cigarettes and other products made or derived from tobacco can be regulated under the Family Smoking Prevention and Tobacco Control Act unless they are marketed for therapeutic purposes, in which case they are regulated as drugs or devices.

On 25 April 2011, the FDA announced that it would abide by the court decision [FDA, 2011]. The announcement went on to delineate a number of controls that the FDA could bring to bear on e-cigarettes and other tobacco products. Among these, there were premarket review requirements for products first marketed or modified after 15 February 2007. Products introduced after that date would need to prove that they are 'substantially equivalent' to products that were on the market on or before 15 February 2007. The unintended consequence of applying this provision to e-cigarettes would be to remove from the market products that have undergone significant improvements, freezing the technology at a stage of development when battery life was too short, vapour production was inconsistent and cartridges leaked [Trtchounian *et al.* 2010]. In addition, the general controls described by the FDA such as registration, product listing, ingredient listing, good manufacturing practice requirements, user fees for certain products, and adulteration and misbranding provisions will all cost money to implement and these costs will, no doubt, be passed on to the consumer. When e-cigarettes first entered the US market, it was more expensive to use an e-cigarette than it was to smoke. Prefilled cartridges tended to last as long as 5 or 10 cigarettes but cost more than half the cost of a pack. As refillable cartridges and refill liquids became available, prices came down and acceptance of the new products grew. Regulation brings with it the potential of a spike in prices that will not only prevent smokers from becoming new e-cigarette consumers but that may also drive a sizable percentage of former smokers back to tobacco smoking.

Overall, the restrictions that some stakeholders wish to impose on e-cigarettes appear to be most

often disguised in the form of the same regulations used for medicinal products. Excessive and ill-conceived regulation will marginalize these products by making them unattractive to smokers and less competitively priced compared with tobacco products by preventing clear communication about reduced risks or by making them hard to access. What is worse, these restrictions are being introduced without taking into account the users' point of view.

For consumers, safety is a concern but secondary in view of the hazards of the product being replaced. Most consumers would be content with safety regulations that helped to assure product consistency and prevent contamination, and labelling that supports making informed buying decisions (e.g. precise specification of nicotine content), but see no need to apply the strict regulations used for pharmaceutical products that would lead to unnecessary increase in products' price [*The Wall Street Journal*, 2010].

Concerns about e-cigarette users increasing their overall intake of nicotine may be misplaced. Surveys consistently find that around two-thirds of e-cigarette users choose nicotine concentrations of over 12 mg/ml [Foulds *et al*. 2011]; however, one study found that using a cartridge labelled as containing 16 mg of nicotine resulted in blood levels of nicotine only one-tenth of the levels produced by smoking [Bullen *et al*. 2010]. Despite the low delivery of nicotine, participants reported that using the 'high nicotine' e-cigarette quelled desire to smoke more effectively.

Another factor that seems to have a positive effect on diminishing desire to smoke is the availability of nontobacco flavours. Etter and Bullen reported that although tobacco flavour had the most users (39%), it was rated lower than all other flavours combined [Etter and Bullen, 2011]. In a web-based survey of over 2000 e-cigarette users, 70.1% reported that they used fruit, beverage or candy-flavoured liquid at least occasionally, and over half reported using these flavours regularly, often or always. In addition, only 27% reported that the availability of such flavours was not influential in their continued use of e-cigarettes [The Consumer Advocates for Smoke-free Alternatives Association, 2010]. Thus, the accusation that only children would want nontobacco flavours appears unfounded.

Ideally, before any regulations are enacted, the regulatory body will require sufficient scientific research to verify that a problem does exist, quantify the problem, explore all potential solutions including making no change at all, determine the possible consequences of each, and then select the solution that is best for public health.

Mitch Zeller, the new director of the FDA Office of Tobacco Products, stated, 'The FDA is committed to making science-based decisions on all product applications and providing the agency's scientific rationale behind its actions to ensure the most transparent and efficient process possible for all involved parties, according to the law' [FDA, 2013b]. Hopefully, other world governments will follow this lead.

E-cigarette regulation recommendations

On the basis of current evidence of benefits and harms relative to tobacco cigarettes and in line with users' desire, future regulatory measures should primarily address quality standards and monitoring of e-cigarettes and e-liquids and should require the following:

(1) evidence that good manufacturing practice (GMP) has been followed;
(2) child-proof caps on fluid containers;
(3) official documentation reporting on the contents of e-cigarette fluids to regulators;
(4) clear, accurate and detailed labelling about the contents and the hazards associated with e-cigarette use.

One such regulatory framework already exists; e-liquids may be marketed as dietary supplements providing no claims about preventing or treating disease are made. Under dietary supplements regulation, manufacturers must indicate a product is not dangerous prior to introduction. Being compliant with national GMP policies is all that is required to ensure that e-liquids are produced in a quality manner: they must not contain contaminants or impurities, they should be accurately labelled, and they must be held under conditions to prevent adulteration. Additional safety principles can be implemented, including a rule requiring that e-liquid manufacturers submit reports of serious adverse events linked to the use of their products. Obviously, the simple scheme of dietary supplements regulation must be integrated by the already existing directives about electronic products safety (for example, in the EU, these classes of products must comply with CE marking and

accompanying Declaration of Conformity before marketing).

Ostensibly, prohibitions on where smoking may take place were enacted to protect the public from exposure to harmful substances in second-hand smoke. Indeed, many such laws include the phrase 'clean air' in the name of the statute. All testing of vapour to date has found no evidence that exhaled vapour produces exposures to contaminants that would warrant health concerns by the standards that are used to ensure safety of workplaces [Cahn and Siegel, 2011; Goniewicz *et al.* 2013]. In addition, there has been no study confirming concerns that the use of e-cigarettes in smoke-free areas might undermine smoke-free laws. Most people have no difficulty differentiating vapour from smoke. Therefore there is no justification for a blanket inclusion of e-cigarettes in existing 'clean air' regulations. Seeing e-cigarettes being used where smoking is prohibited may encourage smokers to make the switch to a product that could save their health and their lives, thereby helping to denormalize smoking by reducing the overall number of smokers.

However, it is reasonable to consider restrictions about e-cigarette use in places frequented by very young children. Likewise, it is prudent to institute controls on marketing of e-cigarettes to nonsmokers and to apply the same prohibition on sales to children and young people as for tobacco products.

Last but not least, if e-cigarettes can be developed to become more reliable and equally as satisfying to smokers as use of tobacco cigarettes, and as readily available and at least as affordable, there will be little incentive for smokers to continue to smoke far more harmful cigarettes. As such, e-cigarettes are not a gateway *to* smoking but a gateway *from* smoking, and heavy regulation by restricting access to e-cigarettes would just encourage continuing use of much unhealthier tobacco smoking.

Concluding remarks

The rationale of tobacco harm reduction is to make nicotine products that are satisfying as a smoking substitute available to smokers at least as easily as cigarettes, and at competitive prices, hence providing all smokers with an easily obtainable lower-risk alternative to smoking. Clive Bates, former director of the UK's Action on Smoking and Health, pointed out that for these alternative products, 'there is place for regulation, but it should be to create an "enabling framework" for these new, much less risky, alternatives to smoking to enter the market in a way that gives consumers confidence in switching from smoking' [Bates, 2012].

Simple regulatory frameworks already exist: e-liquids can be marketed as dietary supplements or as cosmetic products, whereas marketing and safety of e-cigarettes' electronics, batteries and spare parts are already regulated by the existing directives on electronic product design. Therefore, it should be easy to implement a reasonable regulation that is very much in line with consumers' aspirations. Unfortunately, this may be politically impossible to implement because the growing popularity of e-cigarettes is a threat to the interests of the tobacco industry, the pharmaceutical industry and to their associated stakeholders due to the substantial decrease in cigarette consumption and NRT sales. The fat revenues generated by tobacco excise taxes are very much needed by authorities to run their national state and local governments. Fees and investments from the pharmaceutical industry for the marketing of antismoking drugs and medications intended to treat tobacco-related diseases are much needed by regulatory bodies, health authorities and medical societies for the running of their statutory activities.

If these obstacles can be overcome, much misery and suffering can be reduced and millions of lives can be saved.

Funding

DS is expert in Health Communication at the Department of Clinical and Molecular Biomedicine and she is supported by the University of Catania, Italy. GAF is assistant Professor of Constitutional Law at the Department of Law and he is supported by the University of Catania, Italy. RP is full Professor of Internal Medicine with tenure and he is supported by the University of Catania, Italy. RP's research on smoking, electronic cigarettes and tobacco regulation is currently supported by University of Catania and LIAF (Lega Italiana AntiFumo).

Conflict of interest statement

None of the authors have any competing financial interests to declare, with the exception of RP. RP has received lecture fees from Pfizer and GSK, a research

grant from Pfizer, and he served as a consultant for Pfizer, Global Health Alliance for treatment of tobacco dependence, and Arbi Group Srl (the Italian distributor for Categoria electronic cigarettes).

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