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RESEARCH NEWS

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E-Cigarette Dependence: Policies for Product Regulation: Theory, Evidence and Regulatory Policy

This Research News update provides an overview of recent work produced under a grant from Health Canada's Substance Use and Addictions Program (SUAP) on which OTRU is partnering with Physicians for Smoke Free Canada.

Executive Summary

This report focuses on options for e-cigarette product regulations as they pertain to the development of dependence on e-cigarette devices. There are a range of regulatory policies regarding e-cigarette devices and liquids that could curtail development of dependence and possible uptake of smoking by young non-smokers (Table 3). In considering which regulatory policy options to pursue, it is important to consider their likely effects on both young non-smokers and adult smokers. This report outlines evidence, global practice and analysis of nine regulatory policy options regarding three dependence-related mechanisms: sales regulations; e-liquid regulations; and e-cigarette device regulations.

Research Evidence Regarding Dependence on E-Cigarettes

The 2018-19 Canadian Student Tobacco, Alcohol and Drugs Survey reported that current e-cigarette use doubled (20%) among students in grade 7 to 12 since 2016-17, with prevalence highest among students in grade 10 to 12 (29%),[1] with forty percent of e-cigarette youth e-cigarette users reporting daily use. E-cigarette dependence is of concern both as an endpoint and as a determinant of long-term, regular use and its associated potential harms.

Based on a recent review of 25 epidemiological, laboratory and clinical studies, the National Academies of Sciences, Engineering, and Medicine (NASEM) concluded that "*There is substantial evidence that e-cigarette use results in symptoms of dependence on e-cigarettes*".[2] Since the NASEM report, several newer studies provide additional evidence further supporting this conclusion, including a recently published OTRU study.[3]

Jurisdictional Scan of E-Cigarette Product Regulations

Outlined in Table 1, sales regulations can be separated into outright bans, bans on harmful ingredients, and/or regulations on quality of nicotine and/or safety.

Table 1: Sales Regulations

Policy	Country
Ban e-cigarette sales outright	Argentina, Brazil, Brunei Darussalam, Cambodia, Colombia, Egypt, Gambia, India, Iran, Kuwait, Lebanon, Mexico, Mauritius, Nepal, Nicaragua, Oman, Panama, Qatar, Seychelles, Singapore, Sri Lanka, Suriname, Syrian Arab Republic, Thailand, Timor-Leste, Turkey, Turkmenistan, Uganda, and Uruguay
Regulations around sale, such as marketing authorization requirement, cross-border sale restrictions/regulations, restrictions in venues where they can be sold etc.	Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, Fiji, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malaysia, Maldives, Malta, Moldova, Netherlands, New Zealand, Northern Ireland, Norway, Palau, Philippines, Poland, Portugal, Romania, Scotland, Slovakia, Slovenia, Spain, Sweden, Tajikistan, United States, Venezuela and Wales
Ban on all nicotine-containing e-cigarettes	Australia, Jamaica, Japan, Mexico, Sri Lanka and Switzerland

Source: Global State of Tobacco Harm Reduction 2020.

Product regulations, in turn, include the amount of nicotine in e-liquids, bans of ingredients that pose a risk to human health, and regulations on quality of nicotine. Countries may have none, some, or all of these regulations, as noted in Table 2.

Table 2: Product Regulations

Policy	Country
Regulation of amount of nicotine in e-liquids	Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Latvia, Lithuania, Luxembourg, Malta, Moldova, Netherlands, Northern Ireland, Poland, Portugal, Romania, Saudi Arabia, Scotland, Slovakia, Slovenia, Spain, Sweden and Wales
Ban of ingredients that pose a risk to human health in heated or unheated form	Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Moldova, Netherlands, Northern Ireland, Poland, Portugal, Romania, Scotland, Slovakia, Slovenia, Spain, Sweden and Wales
Regulations on quality of nicotine; and/or require products to pass safety and quality evaluations	Austria, Belgium, Bulgaria, Canada, Croatia, Cyprus, Czech Republic, Denmark, England, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, Moldova, Netherlands, Northern Ireland, Poland, Portugal, Romania, Saudi Arabia, Scotland, Slovakia, Slovenia, Spain, Sweden and Wales

Little research has been published on the effectiveness of any of the direct dependence oriented regulatory policies.

Recognizing the difficulty of regulating the inhalation of nicotine by e-cigarette users, researchers have noted the disadvantage to the European Union Directive's 20 mg/ml nicotine concentration limitation highlighting the possibility of increased inhalation to compensate for the lower intake of nicotine.[4,5] This points to the need for regulation that goes beyond nicotine concentration levels to include also regulation of e-cigarette devices to allow for suitable levels of nicotine exposure to users.

There are a range of regulatory policies regarding e-cigarette devices and liquids that could curtail development of dependence and possible uptake of smoking by young non-smokers (Table 3). In considering which regulatory policy options to pursue, it is important to consider their likely effects on both young non-smokers and adult smokers. A more comprehensive analysis, undertaken in the full report, assesses each policy option using four criteria: effect on nicotine use by youth and adults; technical feasibility, political viability and alignment with international trade obligations.

Table 3: Regulatory Policy Options

	Policy Options
Sales regulations	Ban e-cigarette sales outright
	Ban recreational sales/restrict to medicinal use
E-liquid regulations	Ban nicotine e-cigarettes
	Limit nicotine concentration
	Limit size of cartridges/refills
	Prohibit protonated nicotine/ban additives that facilitate inhalation
E-cigarette mechanism regulations	Limit power (heat)
	Regulate length of puff
	Allow only closed systems

Sales Regulations

Ban E-Cigarette Sales Outright

Twenty-nine countries, including Argentina and Brazil, have banned e-cigarette sales. Effects on overall nicotine consumption have not been directly evaluated. There have been no direct comparisons of changes in the prevalence of combustible cigarette use, initiation and cessation between countries that ban and do not ban e-cigarette sales outright.

Ban Recreational Sales/Regulate as a Medicine

Using Singapore as a 50-year simulation model, Doan et al. found that the most effective combination of policies to simultaneously lower risk among current cigarette users while limiting initiation of e-cigarette use among non-smokers, was e-cigarettes on prescription, in combination with minimum legal age requirements and moderate tax rises.[6]

Requiring a prescription for e-cigarettes would restrict the legal market to combustible cigarette smokers. Healthcare professionals could prescribe e-cigarettes as a cessation support and as harm reduction. In theory, this approach would substantially reduce access to nicotine by young non-smokers; however, considering that many young current e-cigarette users are already dependent on nicotine e-cigarettes, it is not unlikely that a thriving illicit market would emerge.

E-Liquid Regulations

Banning and Limiting Nicotine Concentrations

Six countries, including Australia, Japan and Switzerland, allow only non-nicotine e-cigarette product sales. Prior to May 2018, this was also the case in Canada. In Canada, despite this stipulation, nicotine e-cigarettes were widely available. The EU's approach of limiting nicotine concentration to 20 mg/ml seems to have become the standard that other jurisdictions, including some Canadian provinces are adopting. The only hint available of the effects of limiting nicotine concentration to 20 mg/ml is that uptake of e-cigarettes by UK youth is far lower than in the US and Canada which have not adopted this standard. However, the UK approach to

e-cigarette policy differs from the US and Canada in many other respects, including restrictions on advertising and promotion and substantial push from government health organizations of e-cigarettes for smoking cessation and harm reduction. Current evidence does not therefore make it possible to attribute differences between the UK and other countries in youth uptake of e-cigarettes to the 20 mg/ml stipulation.

Indeed, the evidence presented in the full report suggests that even at nicotine concentrations of 20 mg/ml or less users can deliver very high doses of nicotine into their bloodstream by using high power/heat settings on their devices, by using protonated nicotine (nicotine salts), and by puffing longer and harder on the e-cigarette device.

Prohibit Protonated Nicotine/Ban Additives that Facilitate Inhalation

Two countries – France and Iceland – prohibit additives to e-cigarette products that facilitate inhalation. Nevertheless, nicotine salts are still sold in France and there is no evidence available on enforcement or results of restrictions in Iceland. Laboratory studies, reviewed in the full report, demonstrate that lactic acid and other such additives that create nicotine salts allow for high nicotine concentrations to be palatable and for quick and effective effects on the flow of nicotine in the bloodstream to the brain. Even prior to the introduction of protonated nicotine in e-cigarettes, there was considerable evidence that e-cigarette use was associated with dependence. Notwithstanding, since the introduction of protonated nicotine e-cigarette products, use by young non-smokers has increased dramatically and currently a large majority use protonated nicotine with the JUUL brand commanding the largest market share. It is currently not known whether protonated nicotine products are more effective than free-base nicotine products or are necessary for adult smoking cessation and harm reduction.

E-Cigarette Device Regulations

Limit Power/Heat, Regulate Length of Puff, Allow Only Closed Systems

E-cigarette designs, heating element features, liquid contents, and user behavior all individually have limited utility as metrics of inhalation-related nicotine exposure, toxicity, and effectiveness.

The utility of these individually considered features is limited because no one feature alone determines the rate at which nicotine is emitted (i.e., the flux). For instance, a high-voltage/low nicotine concentration combination may provide the same or greater flux as a low-voltage/high nicotine concentration combination. The flux, as a result, determines the effect of a given nicotine dose, ranging from no effect to acute toxicity. If the e-cigarette nicotine flux is low, users likely will abandon the device. If the flux is high (e.g., exceeds levels characteristic of combustible cigarettes), users may accept the device despite the fact that it carries with it the potential for toxic side effects.[7]

As users might compensate for limited power by taking longer puffs, restrictions on power/heat might be accompanied by requiring that devices have a mechanism that automatically shuts off after x seconds of a puff. Restricting devices to closed systems with heat and puff limitations set at the factory would facilitate power/heat and puff length stipulations. To limit the dependence risk, policymakers could consider prohibiting e-cigarette devices that allow for high power/heat. Limits on power/heat are not currently in place in any jurisdiction that we are aware of.

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Full publication available on request. Email publications@otru.org with the name of the publication you're requesting.

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