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## The case for the WHO Advisory Note, Global Nicotine Reduction Strategy

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### INTRODUCTION

Cigarettes are the most addictive tobacco product and also the most deadly, causing the highest rates of tobacco-caused mortality and morbidity in most areas of the world.<sup>12</sup> Although current tobacco control efforts have led to significant reductions in smoking prevalence, innovative strategies that can result in a more rapid elimination of cigarette smoking should be a high priority.<sup>13</sup> In the US Surgeon General's report,<sup>1</sup> reducing nicotine in cigarettes was considered as one potential strategy. In an article written by Tengs *et al*,<sup>4</sup> in which the authors modelled the effects of reducing nicotine in cigarettes on public health, taking into account a potential black market, the following statement was made: 'Policy makers would be hard-pressed to identify another domestic public health intervention, short of historical sanitation efforts, that has offered this magnitude of benefit to the population'. Hence, the main goal of the Advisory Note, Global Nicotine Reduction Strategy, issued by the Study Group on Tobacco Product Regulation (TobReg), was to provide a scientific review and examine the potential feasibility of reduced nicotine content cigarettes as an approach to tobacco control, and to describe the context in which this approach could be considered. This approach is bold, but worth serious consideration. Why? Because the tobacco control community has known for decades that the harms associated with smoking are primarily driven by its addictiveness. If the reinforcing effects of a drug are reduced, then continued use and consequently toxicant exposures will substantially diminish. However, this strategy is not suitable for all countries. As acknowledged in the article, Cigarette prohibition and the need for more prior testing of WHO TobReg's global nicotine-reduction strategy, written by Dr Kozlowski, many cautionary notes and caveats were raised in the TobReg report regarding a mandate to reduce nicotine in cigarettes. Each country would

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need to consider the impact of this approach on smuggling, enforcement, the use of alternative nicotine products and their toxicity, and resources necessary to implement and to monitor this policy.

## CIGARETTE PROHIBITION OR SAVING LIVES?

One of the main issues raised in Kozlowski's article is whether or not reducing nicotine in cigarette products is in fact cigarette prohibition. Furthermore, he states that 'recommending FCTC (Framework Convention on Tobacco Control) countries adopt a nicotine-reduction strategy demonstrates relatively little concern for possible negative societal consequences', which were observed as a result of alcohol prohibition. The intent of reducing nicotine content in cigarettes is not to prohibit cigarettes, but to reduce the addictiveness of cigarettes so that people have a choice as to whether or not they want to continue using an extremely toxic product. At the same time, less toxic nicotine delivery products could be made available. The TobReg Advisory Note states, 'Policy approaches could be considered to motivate smokers who are unable to quit to substitute less hazardous forms of tobacco and nicotine use...in order to encourage complete cessation of use of the more toxic product (page 24)'. Furthermore, the Advisory Note states, 'Both the appeal of reduced nicotine cigarettes and the availability and appeal of alternative forms of nicotine are likely to affect the extent of illicit sales (page 23)'. Therefore, unlike alcohol prohibition, smokers will still have access to nicotine but in less harmful delivery systems and this availability would minimise their efforts to seek nicotine through illegal means. A policy that makes cigarettes—which lead to about half a million deaths per year in the USA and 6 million worldwide—less satisfying and appealing is not unreasonable. Products that kill people are often prohibited from being sold to consumers. Using the tea example provided by Dr Kozlowski, if coffee but not tea was found to kill half its consumers, a government would be considered negligent if it knowingly and freely allowed this product to be addictive and made available to consumers.

Dr Kozlowski raised concern over the toxicity of alternative tobacco products. The Advisory Note also stated that 'Substitution of alternative products could have adverse effects or maintain addiction in a significant segment of the population. Therefore, a successful nicotine reduction policy must be supported by a comprehensive regulation of all tobacco- and nicotine-containing products (page 24)'. The goals of this regulation would be to 'minimise highly toxic nicotine-containing products and to monitor the health effects of these less toxic products'.

## HOW MUCH SCIENCE DO WE NEED?

Dr Kozlowski also indicated that the authors of a large trial examining the impact of reduced nicotine content cigarettes stated that the results of past and current studies are 'suggestive' of the beneficial outcomes of nicotine reduction.<sup>5</sup> However, multiple studies, albeit some with small sample sizes, have consistently shown that very low nicotine content (VLNC) cigarettes reduce the number of cigarettes smoked, decrease dependence and/or increase quit attempts compared to continued use of normal or moderately lower nicotine content cigarettes.<sup>5-10</sup> Furthermore, there is evidence of neither compensatory smoking<sup>511</sup> nor

serious adverse events.<sup>5</sup> The clinical significance of the statistically reliable effects observed in the study by Donny *et al*<sup>5</sup> was called into question. However, it is notable that the prevalence of quit attempts in the VLNC cigarette condition versus normal nicotine content condition was 34.7% versus 17% in a population of smokers who were not motivated to quit smoking at the entry of the study. Also notable is that reduction in smoking and dependence was observed even though this population was provided free cigarettes and had access to cigarettes that are highly addictive. In a world with limited availability to highly addictive cigarettes and where the cost of cigarettes is high, one would presume a greater decrease in dependence and that a greater number of cigarette quit attempts would be observed. In the study conducted by Donny *et al*,<sup>5</sup> an additional analysis of data showed that over half of the participants in the low nicotine groups indicated they would quit smoking in a year if these were the only type of cigarettes available for purchase (T Smith, R Cassidy, J Tidey, *et al*. Impact of smoking reduced nicotine content cigarettes on sensitivity to cigarette price: Results from a multi-site clinical trial. Under review, 2016).

Dr Kozlowski is correct to say that the impact of nicotine reduction on vulnerable populations (eg, smokers with physical or mental illness or substance abuse problems) is not clearly known; numerous studies are ongoing that examine these populations and scheduled to be completed within the next few years. The Regulatory Recommendations section in the TobReg Advisory Note, however, states, ‘The availability of effective, affordable cigarette cessation treatment, alternative forms of nicotine, optimal medicinal forms of nicotine and other approved treatments and medicines for tobacco dependence and withdrawal will help dependent smokers who experience adverse effects or withdrawal symptoms (page 29)’. Shifting these vulnerable populations away from dangerous products by providing accessible and affordable smoking cessation treatments or less harmful products would seem to be an urgent need because of the high rates of cigarette-caused mortality and morbidity experienced by these populations.

## CONCLUSION

If the TobReg Advisory Note catalyses a country with ‘extensive, effective and comprehensive’ tobacco control programmes and sufficient resources to implement a policy to substantially reduce nicotine in cigarettes (and preferably all combusted products), this note would have served its purpose. With adequate surveillance of the impact of this approach, other countries could potentially learn from this country’s pioneering experience. Allowing this idea to sit on the shelf when it has the potential to save millions of lives would be a travesty.

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## REFERENCES

1. U.S. Department of Health and Human Services. The health consequences of smoking—50 years of progress: a report of the surgeon general. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2014.

2. Eriksen M, Mackay J, Schluger N, et al. The Tobacco Atlas, 5th edn, Atlanta, GA, American Cancer Society, Inc, 2015; p 15.
3. Warner KE. An endgame for tobacco? *Tob Control* 2013;22(Suppl 1):i3–5. [PubMed: 23591502]
4. Tengs TO, Ahmad S, Savage JM, et al. The AMA proposal to mandate nicotine reduction in cigarettes: a simulation of the population health impacts. *Prev Med* 2005;40:170–80. [PubMed: 15533526]
5. Donny EC, Denlinger RL, Tidey JW, et al. Randomized trial of reduced-nicotine standards for cigarettes. *N Engl J Med* 2015;373:1340–9. [PubMed: 26422724]
6. Hatsukami DK, Kotlyar M, Hertsgaard LA, et al. Reduced nicotine content cigarettes: Effects on toxicant exposure, dependence and cessation. *Addiction* 2010;105:343–55. [PubMed: 20078491]
7. Hatsukami DK, Heishman SJ, Vogel RI, et al. Dose-response effects of spectrum research cigarettes. *Nicotine Tob Res* 2013;15:1113–21. [PubMed: 23178320]
8. Donny EC, Jones M. Prolonged exposure to denicotinized cigarettes with or without transdermal nicotine. *Drug Alcohol Depend* 2009;104:23–33. [PubMed: 19446968]
9. Benowitz NL, Hall SM, Stewart S, et al. Nicotine and carcinogen exposure with smoking of progressively reduced nicotine content cigarette. *Cancer Epidemiol Biomarkers Prev* 2007;16:2479–85. [PubMed: 18006940]
10. Benowitz NL, Dains KM, Hall SM, et al. Smoking behavior and exposure to tobacco toxicants during 6 months of smoking progressively reduced nicotine content cigarettes. *Cancer Epidemiol Biomarkers Prev* 2012;21:761–9. [PubMed: 22354905]
11. Hatsukami DK, Donny EC, Koopmeiners JS, et al. Compensatory smoking from gradual and immediate reduction in cigarette nicotine content. *Cancer Epidemiol Biomarkers Prev* 2015;24:472–6. [PubMed: 25515551]