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Ending tobacco-caused mortality and morbidity: the case for performance standards for tobacco products

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ABSTRACT

The US Family Smoking Prevention and Tobacco Control Act and WHO Framework Convention on Tobacco Control provide us with powerful tools to reduce the death and disease caused by the use of tobacco products. One tool that can contribute substantially toward this goal is the authority to establish performance standards for tobacco products. Conjointly with reducing levels of nicotine in cigarettes, performance and quality control standards need to be established for non-combusted tobacco products. Performance standards and incentives should be provided so that tobacco companies are compelled to manufacture and market products with very low or almost non-existent toxicity (eg, nicotine-only products).

COMMENTARY

As described in a paper summarising the proceedings of a strategic dialogue on tobacco harm reduction,¹ there is a continuum of risk for tobacco products with combustible products associated with the highest health risk, and pure nicotine delivery products (primarily medicinal nicotine) associated with the lowest risk. To improve public health, one potential 'endgame' goal would be to gradually move the population of tobacco users from the highest to the lowest risk product, with the eventual goal of making the population tobacco free. How can this be achieved?

One of the most powerful tools in the US Food and Drug Administration Family Smoking Prevention and Tobacco Control Act to substantially improve public health is the regulatory authority to establish performance standards for tobacco products. It is also a powerful tool provided in Article 9 ('Regulation of Contents of Tobacco Products') of the Framework Convention on Tobacco Control. The following describes a potential scenario of how performance standards for tobacco products, which, heretofore, have not been a primary focus for the tobacco control community, can be used as one of the means to shift the population away from the most deadly nicotine-containing products, and to reduce tobacco-related mortality and morbidity.

Scientific literature suggests that reducing nicotine in cigarettes to a specific level (most likely less than 1 mg nicotine content) can result in a significant reduction in cigarette smoking and may facilitate abstinence.²⁻⁵ This dose of nicotine has not been associated with clinically significant increases in withdrawal symptomology, significant compensatory smoking behaviour, nor greater exposure to tobacco carcinogens or increased cardiovascular risk factors. When the cigarette is also reduced in

tobacco carcinogen levels, a significant reduction was observed in exposure to these carcinogens,⁴ thereby supporting the importance of reducing both the nicotine and toxicants in cigarettes. The sample sizes in these studies were relatively modest, pointing to the need for larger trials determining the dose that is likely to eliminate smoking (because in the USA, the dose cannot be reduced to zero) with relatively minimal adverse consequences (significant physiological, cognitive or psychological discomfort), ways to mitigate these effects, the best approach to reducing levels of nicotine on a national level, and ensuring that vulnerable populations of smokers (eg, individuals with comorbid psychiatric disorders) are not unduly affected. Other performance standards may also be considered to reduce the appeal of the product such as elimination of non-characterising flavorants, eliminating specific design features of cigarettes that enhance better particle deposition in the lungs or requiring a specific pH level in the cigarette.⁶ Instituting these performance standards would require a significant surveillance system to track any unintended consequences,⁶⁻⁸ and to mitigate them as best we can.

If sufficient science is generated to support reducing levels of nicotine in cigarettes and other combustible products, then we are left with the question of what to do with non-combusted tobacco products. To minimise initiation (serving as a starter product as described by Connolly⁹), a performance standard of high rather than low nicotine may be considered along with a ban on flavorants.¹⁰ Additionally, because of the substantial variability of toxicants in smokeless tobacco products within and across different countries,¹¹⁻¹³ performance standards for toxicants in these products are needed (regardless of whether or not nicotine in cigarettes is reduced). There are already known ways to reduce toxicant levels in oral tobacco products including use of specific tobacco leaves, curing and manufacturing processes that could easily be implemented.¹¹ Studies have shown that oral tobacco products that are reduced in toxicants are associated with negligible increases in oral cancers, pulmonary disease and non-fatal cardiovascular disease.¹⁴⁻¹⁶ Nonetheless, reduced toxin oral tobacco products are not harmless and may be associated with fetal toxicity, increased risk of fatal cardiovascular disease and pancreatic cancer.^{14 15 17} Ultimately, tobacco users need to be shifted towards a cleaner form of nicotine delivery.

Reducing nicotine in cigarettes, establishing increasingly strict standards for toxicants in non-combusted tobacco products, and establishing standards to make all tobacco products less appealing, may facilitate the development of less harmful

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methods of nicotine delivery by the industry, including devices or products that rapidly deliver nicotine without the toxicants. Products of high abuse potential (eg, pulmonary delivery of nicotine), sold only by prescription, could be used to substitute completely for cigarettes. On the other hand, nicotine used in a form without high abuse potential may be acceptable for prolonged or occasional use and made more accessible to consumers because persistent use is not likely to result in significant death and disease.^{16–18} Even if all smokers switched to rapid pulmonary delivery of nicotine, public health benefit may be observed.¹⁹

Innovations from industry may also take the form of research that contributes to a better understanding of the effects of nicotine on different nicotinic receptor subtypes. With increasing stringent performance standards, it is possible that tobacco companies will eventually evolve into developing pharmaceuticals (ie, Targacept) that target specific nicotinic receptors that have specific functional value (eg, nicotinic receptors such as $\alpha 4\beta 2$ or $\alpha 7$ for learning and memory, neuroprotective, antinociception or anxiolytic and antidepressant effects^{20–24}).

In summary, the vision is a world in which consumers are not using products that have levels of constituents that lead to death and disease. Although this approach may not be appropriate for all countries, regulating tobacco constituents is an approach worth serious consideration.

Competing interests None.

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REFERENCES

- Zeller M, Hatsukami D. The strategic dialogue on tobacco harm reduction: a vision and blueprint for action in the US. *Tob Control* 2009;18:324–32.
- 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.
- 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.
- Hatsukami D, Kotlyar M, Hertzgaard LA, et al. Reduced nicotine content cigarettes: effects on toxicant exposure, dependence and cessation. *Addiction* 2010;105:343–55.
- Walker N, Howe C, Bullen C, et al. The combined effect of very low nicotine content cigarettes, used as an adjunct to usual Quitline care (nicotine replacement therapy and behavioural support), on smoking cessation: a randomized controlled trial. *Addiction* 2012;107:1857–67.
- Hatsukami D, Perkins KA, Lesage MG, et al. Nicotine reduction revisited: science and future directions. *Tob Control* 2010;19:e1–10.
- Hatsukami DK, Benowitz NL, Donny E, et al. Nicotine reduction: strategic research plan. *Nicotine Tob Res* Published Online First: 25 Oct 2012. doi:10.1093/ntr/nts214
- Henningfield JE, Benowitz NL, Slade J, et al. Reducing the addictiveness of cigarettes. Council on Scientific Affairs, American Medical Association. *Tob Control* 1998;7:281–93.
- Connolly GN. The marketing of nicotine addiction by one oral snuff manufacturer. *Tob Control* 1995;4:73–9.
- Oliver AJ, Jensen JA, Rogel RI, et al. Flavored and nonflavored smokeless tobacco products: rate, pattern of use, and effects. *Nicotine Tob Res* 2012;15:88–92.
- Stanfill SB, Connolly GN, Zhang L, et al. Global surveillance of oral tobacco products: total nicotine, unionised nicotine and tobacco-specific N-nitrosamines. *Tob Control* 2011;20:e2.
- Stepanov I, Jensen J, Hatsukami D, et al. New and traditional smokeless tobacco: comparison of toxicant and carcinogen levels. *Nicotine Tob Res* 2008;10:1773–82.
- Richter P, Hodge K, Stanfill S, et al. Surveillance of moist snuff total nicotine, pH, moisture, un-ionized nicotine, and tobacco-specific nitrosamine content. *Nicotine Tob Res* 2008;10:1645–52.
- International Agency for Research on Cancer. Smokeless tobacco and some tobacco-specific nitrosamines. *IARC monographs on the evaluation of carcinogenic risks to humans*. Lyon, France: IARC, 2007:89.
- Boffetta P, Straif K. Use of smokeless tobacco and risk of myocardial infarction and stroke: systematic review with meta-analysis. *BMJ* 2009;339:b3060.
- Royal College of Physicians. Harm reduction in nicotine addiction: helping people who can't quit. *A report by the Tobacco Advisory Group of the Royal College of Physicians*. London: Royal College of Physicians, 2007.
- Boffetta P, Hecht S, Gray N, et al. Smokeless tobacco and cancer. *Lancet Oncol* 2008;9:667–75.
- McNeill A, Foulds J, Bates C. Regulation of nicotine replacement therapies (NRT): a critique of current practice. *Addiction* 2001;96:1757–68.
- Sumner W II. Estimating the health consequences of replacing cigarettes with nicotine inhalers. *Tob Control* 2003;12:124–32.
- Piccio MR, Brunzell DH, Caldarone BJ. Effect of nicotine and nicotinic receptors on anxiety and depression. *Neuroreport* 2002;13:1097–106.
- Piccio MR, Caldarone BJ, King SL, et al. Nicotinic receptors in the brain. Links between molecular biology and behavior. *Neuropsychopharmacology* 2000;22:451–65.
- Levin ED, McClernon FJ, Rezvani AH. Nicotinic effects on cognitive function: behavioral characterization, pharmacological specification, and anatomic localization. *Psychopharmacology* 2006;184:523–39.
- Cordero-Erausquin M, Marubio LM, Klink R, et al. Nicotinic receptor function: new perspectives from knockout mice. *Trends Pharmacol Sci* 2000;21:211–7.
- Mudo G, Belluardo N, Fuxe K. Nicotinic receptor agonists as neuroprotective/neurotrophic drugs. Progress in molecular mechanisms. *J Neural Transm* 2007;114:135–47.