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Commentary

Prospects for a nicotine-reduction strategy in the cigarette endgame: Alternative tobacco harm reduction scenarios

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ABSTRACT

Some major national and international tobacco control organisations favour mandating a reduction in nicotine content of cigarettes to non-addictive levels as a tobacco control tool. Reducing nicotine content, it is argued, will make tobacco smoking less attractive. The 2009 U.S. Food and Drug Administration's regulation of cigarettes appears to have the power to reduce nicotine to non-addictive levels provided it is not taken to zero. A consideration of the U.S. context, however, raises doubts about (a) whether this will ever be practicable and (b), if practicable, how long it will take to implement. Current versions of the nicotine-reducing strategy propose the systematic, incentivised use of less harmful nicotine/tobacco products as elements of the mandatory cigarette nicotine-reduction strategy. Time will tell if and when mandatory nicotine reduction in tobacco cigarettes will occur and what impact it might have on smoking prevalence. The question posed here is "Why wait?" Resources used in implementing reduction in nicotine content have an opportunity cost. In the meantime, nicotine-maintaining harm reduction strategies can have nearer term effects on tobacco use as an individual and a public health issue.

The low-nicotine cigarette strategy

An innovative proposal made in 1994 (Benowitz & Henningfield, 1994) to mandate sales only of non-addictive, low-nicotine tobacco cigarettes has had a dominant place in cigarette endgame strategies and is encouraged by the American Medical Association, the British Medical Association, the U.S. Food and Drug Administration (FDA) and the U.S. Surgeon-General (Benowitz & Henningfield, 2013; Hatsukami, Benowitz, Donny, Henningfield, & Zeller, 2013; National Center for Chronic Disease Prevention and Health Promotion, 2014). The WHO framework convention on tobacco control (FCTC) is also supportive (Gray & Borland, 2013). Part of the appeal of the non-addictive cigarette may be its direct attack on addiction (Kozlowski, 2013), and its elimination of "gateway" issues by removing conventional cigarettes as a product option. Research agendas for reduced-nicotine have been proposed (Donny et al., 2014; Gray & Borland, 2013). In its full form the proposal argues for research, government regulation, gradual reduction, consumer education, and increased availability of lower-risk options (Benowitz & Henningfield, 2013). The 2009 United States FDA tobacco law makes the strategy seem within reach by including the authority to reduce nicotine in cigarettes, provided levels are not taken to "zero" and by creating resources for research (United States Code, 2009).

The proposal has been criticised (e.g., Jarvis & Bates, 1999; Joossens & Hayes, 1999; Shatenstein, 1999), but overall there has been enthusiastic, high-level support. This article argues that examination of the U.S. situation shows that (a) the strategy may not be practicable, given other provisions of the FDA law and centrality of addictive-levels of nicotine to the popularity of cigarettes and (b), if practicable, it will likely take many years to implement. Optional low-nicotine cigarettes are expected to continue to exist with small markets, but failing to require such cigarettes would represent significant failure for the strategy. There are substantial opportunity costs from resources committed to a strategy that could be impracticable or in the distant future, rather than to other product-focused strategies that may be more practical, involving pleasurable, safer forms of nicotine use such as vaping (electronic cigarettes) or some smokeless tobaccos such as snus (Royal College of Physicians, 2007, 2014).

FDA regulation

Since 2009, the FDA Act "... aims to curb the trend of new users becoming addicted before they are old enough to understand the

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risks and ultimately dying too young of tobacco-related diseases," (U.S Food and Drug Administration, 2013b) and regulations are "narrowly tailored" to restrict promotion to youth, "while affording tobacco manufacturers and sellers ample opportunity to convey information about their products to adult consumers" (Sec 2–32). FDA law protects cigarettes by (a) forbidding banning (b) specifying that a consideration in requiring product changes is creation of contraband markets, and (c) sheltering cigarettes from competing marketing of less-dangerous products by means of an expensive evaluation process with broad, difficult-to-measure requirements that new products should not have negative population effects. FDA law compels evaluation of the nicotine-reduction strategy. Nicotine-manipulated cigarettes have been purchased for research, and $2.5 million allocated for year one of a 5-year research project on low-nicotine cigarettes (Wilson, 2011a). A well-funded research domain, "Tobacco Regulatory Science," has burgeoned within the National Institutes of Health (NIH) from manufacturer fees paid to FDA (Leischow, Zeller, & Backinger, 2012) that fund, e.g., 14 Tobacco Centers of Regulatory Science at $270 million over 5 years (U.S Food and Drug Administration, 2013a).

The FDA succeeded in banning flavoured cigarettes (but not menthol in cigarettes). The FDA also succeeded in banning "light" and "mild" brand descriptors, however the products themselves did not change and colour-coding can still guide consumers (Connolly & Alpert, 2014). The "lighter" products also are associated with a milder taste that still can contribute to consumers perceiving them as less dangerous than stronger cigarettes (Kozlowski & O'Connor, 2002).

One explicit strategy in FDA law was advanced in 2011 and required colour graphic warning labels (Campaign for Tobacco-Free Kids, 2014); however, the industry prevented this in court (Wilson, 2011b), and the FDA in the end abandoned further legal review. One issue influencing the ruling was the government's own cost-benefit analysis (obligatory for all federal agencies) in which "lost pleasure" to smokers was included as a significant "cost" of regulation (Chaloupka, Gruber, & Warner, 2014; Song, Brown, & Glantz, 2014). At present, no graphic warnings are required, and creating labels preserving 'freedom of commercial speech' issues will take more research and probably meet further lawsuits. In another lawsuit on product regulation, the judge ordered that FDA reconstitute its advisory committee because of conflict-of-interest issues and barred use of findings on menthol cigarettes (Rosenberg, 2014). It is clear that unwelcome FDA actions will be opposed by industry and can lead to blocking of FDA actions.

Challenges to *Mandating* low-nicotine cigarettes

Despite the weight of optimistic official support, several factors argue that *required* low-nicotine cigarettes may not be achievable or will be problematic because of the years it would take to implement. The issue is not whether low-nicotine cigarette will be marketed. They have been, are, and likely will continue to be marketed. The doubt is whether or when they can become the only legal cigarette on the market, no matter what is written in one part of a complex law.

Cigarettes with low nicotine-content tobacco have been tried commercially with very limited success (Dunsby & Bero, 2004). Some failures could have been caused by removal of too much nicotine or by early processes used to reduce nicotine having taste issues. Overall, tobacco addiction experts would expect that low-nicotine content cigarettes would disappoint many smokers, given compensatory smoking that occurs with conventional "lower-yield" cigarettes containing plenty of nicotine (e.g., National Cancer Institute, 2001). Nicotine has long been recognized as a central component of cigarette smoking (e.g., Henningfield & Fant, 1999). From 2003 to 2009 Quest® cigarettes were marketed with three different nicotine levels (Becker, Rose, & Albino, 2008; Catanzaro et al., 2007; Cobb, Weaver, & Eissenberg, 2010; Hammond & O'Connor, 2014; Paradise, 2013; Parascandola, Augustson, O'Connell, & Marcus, 2009; Penetar, Lindsey, Peters, Juliano, & Lukas, 2012; Perkins & Karelitz, 2013; Shadel et al., 2006; Strasser, Lerman, Sanborn, Pickworth, & Feldman, 2007; Strasser, O'Connor, Mooney, & Wileyto, 2006; Strasser, Tang, Tuller, & Cappella, 2008; Walker et al., 2011). These cigarettes employed the same patented processes (owned by 22nd century group) to genetically-alter nicotine in tobacco that is used in the cigarettes supplied to NIH. Analysts wrote: "A large tobacco company spent $25 M on advertising for Quest-branded modified nicotine cigarettes, before giving up on the product" (Seeking Alpha, 2014). Other reviewers have noted these cigarettes were not popular (McNeill, Hammond, & Gartner, 2012).

Altria (owner of Philip Morris USA) supported the 2009 legislation (Wilson, 2009b). In contrast, Philip Morris led opposition in a $40 million campaign against a previous bill (Wilson, 2009a). Corporate responsibilities stress increasing profits rather than losing profits. Altria helped write the successful bill (Wilson, 2009a) and surely assessed long-term prospects for litigation and implementation.

Consider how consumers and sellers of caffeinated coffee/tea, cannabis (in Colorado or Oregon in the U.S. where legal), or beverage alcohol would react to proposals to reduce drug levels to "above zero," but low psycho-activity levels. It would be treated as a prohibition of the "real" product and an unfair alteration of a popular product. Interestingly, alcohol prohibition in the U.S. was fundamentally a low-alcohol proposal directed at "intoxicating liquors." Many Americans were said to have expected that beer and wine would still be allowed, and were shocked when the Volstead Act defined "intoxicating liquors" as anything with >5% alcohol in keeping with tax laws (Goodwin, 2014).

Companies could fight (within the FDA law) on grounds that it constitutes *de facto* banning of cigarettes. There is also the question of how "not-zero" nicotine should be defined – as a chemical test or having enough nicotine to function as a traditional cigarette. What judgments will be applied to contraband markets (of concern to both FDA law and the industry)? Analyses for warning labels weighed "lost pleasure" to former and would-be smokers (Chaloupka et al., 2014); such analyses here could also estimate "lost pleasure" to current smokers. Major corporations can influence government. Political makeup of the Congress can also change future FDA regulation. (Congressional leaders, e.g., are now "pushing back on pending regulations" on e-cigarettes (Nelson, 2014).)

Yes, but the companies don't always get what they want

Of course, tobacco companies have had to deal with regulations they don't like. They have opposed tax increases on their products, but such increases have been implemented. The cigarette companies may be reassured by the price-elasticity of cigarettes, and they also often have ways to decrease prices to consumers. Though increased taxes are an effective tobacco control strategy, they also contribute to a government's "dependence" on the continued sale of tobacco as a source of revenue (Gilmore, Tavakoly, Taylor, & Reed, 2013; Golden, Ribisl, & Perreira, 2014; Jiang & Ling, 2013). The mandatory nicotine-reduction strategy may be different in that it is a direct adulteration of the product. Higher taxes, public smoking bans, banning of light/mild descriptors may be tolerable by the industry largely because the desirable, psychoactive, addictive product is unchanged. (By analogy, consumers will pay high prices for highly-taxed Scotch, but probably wouldn't if the Scotch had only low levels of alcohol.) Reducing nicotine to non-addictive

levels is likely to be a make or break issue for the industry, because significant, psychoactive levels of nicotine that can lead to addiction have been a central feature historically of all successful tobacco products (Kozlowski, 1982).

If practicable, it is still years from implementation

Many experts will maintain optimism for the low-nicotine strategy, but they should agree that, if it does happen, it would easily be 5, 10, or many more years off. Beyond delays caused by the intrinsically slow process of development of formal regulations and processing comments on them (and legal challenges), there would be delays from a gradual phase-down of nicotine. Companies could occupy years of testing effects of (and safety of) various techniques for creating low-nicotine tobacco, if they don't want to employ the current patented process for nicotine reduction. Also, parallel implementation of low-nicotine cigar requirements would be needed and require research (and it would also be fought). And the FDA does not yet have jurisdiction over cigars. Many disappointed cigarette smokers would switch to cigars (little or big) as has happened with changes in differential taxes (Government Accountability Office, 2012; Warner & Pollack, 2014). At 480,000 annual premature deaths (Centers for Disease Control, 2014) from smoking, years of delay for a nicotine-reduction strategy to take effect could have grave mortality effects.

Urgent need for support of reduced harm products

Combustibles are by far the most harmful tobacco products (National Center for Chronic Disease Prevention and Health Promotion, 2014; Royal College of Physicians, 2007). Nicotine in doses typically ingested by tobacco users is not harmless but considerably less harmful than tobacco smoke (Royal College of Physicians, 2007). The nicotine-reduction strategy has endorsed the use of less harmful tobacco/nicotine products, supported by differential tax incentives, in concert with the implementation of mandatory nicotine-reduction in cigarettes (Benowitz & Henningfield, 2013). Products like snus and e-cigarettes would qualify as significant harm-reduction products (Hajek, Etter, Benowitz, Eissenberg, & McRobbie, 2014; Kozlowski, 2007).

Clearly, there are complexities in that the tobacco industry may seek to hijack the harm reduction approach paradoxically to promote greater use of combustible tobacco. However, the policy challenges to addressing these may be inherently more tractable than trying to force the industry to ruin their core product. Attempts to undermine this kind of harm reduction approach by trying to mislead the public and policy makers about the harms of smokeless tobacco and electronic cigarettes can play into the hands of the tobacco industry by fostering business as usual for deadly cigarettes.

The American Heart Association's recent policy on electronic-cigarettes speculates that e-cigarettes might be a useful substitute for cigarettes once FDA's low-nicotine cigarette strategy, coupled with higher taxes on cigarettes, pushes smokers away from cigarettes, but they note: "... it remains unclear whether society would be accepting of recreational nicotine addiction if associated with minimal health consequences" (Bhatnagar et al., 2014). Such speculation resonates with irony: Society currently tolerates addictive and deadly cigarettes! (Gallup, 2014). But more importantly, one wonders why it is important to wait for the mandatory low-nicotine cigarette. The evidence on snus as a reduced harm product is clear (Scientific Committee on Emerging and Newly Identified Health Risks, 2008). The Swedish experience of snus demonstrates that it is possible to avoid a gateway from snus to cigarettes (Scientific Committee on Emerging and Newly Identified Health Risks, 2008), but the marketing of the relative dangers of snus and cigarettes may be a key part of this (Lund & Scheffels, 2014) as well as differential costs. The population does need to be informed about the relative risks of different products (Kozlowski & Edwards, 2005; Meier & Shelley, 2006).

Limiting sales to only low-reinforcement cigarettes are a "stick" to beat consumers to alternative nicotine-delivery systems. It could be better to support less dangerous "carrot" like e-cigarettes and vaping products with substantial nicotine that could attract smokers away from cigarettes. The growing "voluntary" sales of vaping products with ample nicotine levels suggests this is happening (Friedman, 2014). Standard marketing principles (the 4-Ps: price, promotion, product, place (Goi, 2009; Dewhirst & Lee, 2012)) can be used to support the movement from cigarettes to these products. If cigarettes were to lose to competitors in the marketplace, this would avoid some of the challenges of trying to impose governmental regulations.

The movement to low-nicotine cigarettes has become part of tobacco endgame projections (Daynard, 2013; Warner & Pollack, 2014), and is supported by an FCTC article and FDA regulation. A scientifically-reasoned plan for requiring low-nicotine cigarettes does have comforting features that could allay tobacco control concerns. Imagine a well-controlled world of educated, well-comported consumers with no gateway fears because of the elimination of the deadly, addictive, pleasurable product that is the gateway terminus. This hypothetical world contains mostly safe, pharmaceutically-vetted products used almost exclusively by adults and with only inconsequentially small black markets. Research on moral psychology has shown that, when there are violations of a sense of community standards and respect for authority, the emotional responses of disgust and contempt are triggered (Kozlowski, 2013). This hypothetical world is one where the moral psychological responses of disgust of and contempt for the state of affairs would be low.

However, youth has been the time of recruitment to many products forbidden to youth. In 2013 (Johnston, O'Malley, Schulenberg, & Miech, 2014), 39% of U.S. high school seniors reported some alcohol use in the past 30 days and 26% reported having been drunk; 16% of seniors reported smoking a cigarette in the past month. (And 23% of 12th graders reported marijuana/hashish use in the past 30 days which is not yet legal for most adults in the United States.) Will adventurous youth sneak ersatz cigarettes or the "hard stuff"? (Youth can prefer the "hard stuff" for alcohol (Siegel, Naimi, Cremeens, & Nelson, 2011)). A contrasting hypothetical worldview would see less orderly behaviour in the use of multiple recreational substances, along with great corporate Leviathans ruling commercial seas, and with susceptible governments with complex, self-contradictory, imperfectly-enforceable laws, and a populace, whether young or old, that wants what the populace wants, whether from black or grey or white markets.

Even if one's worldview lies between these caricatures, one should consider whether or when the intellectual and financial investments in the low-nicotine content strategy will pay off. No matter FCTC or FDA, any government lacking the power to ban cigarettes may in effect lack the power to ban addictive levels of nicotine in cigarettes. Product-focused tobacco control should be actively working to minimize harm from tobacco products in order to deal with the cigarette health emergency (Sweanor, Alcabes, & Drucker, 2007), while the popular strategy of mandatory cigarette nicotine reduction is being pursued. Should that strategy materialize down the road, it will likely face a smaller cigarette market.

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