



Time for major roadworks on the tobacco road?

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Nicotine replacement

Inhaling tobacco smoke is a remarkable and exquisitely refined mechanism for delivering nicotine to the central nervous system. Remarkable for its acute safety and chronic catastrophe, and unique because it is tobacco (not nicotine) that causes the damage. The failure to make this crucial distinction is a tragedy.

Alternative methods of delivering nicotine via tobacco have been available for centuries in the form of chewing tobacco, snuff, drinks, enemas, and percutaneous administration—all developed by the aboriginal peoples of North and South America.^{1,2}

In 1942, Johnston administered nicotine intravenously to himself and 34 volunteers thus altering smoking behaviour in recipients.³ Further development of alternative nicotine delivery took another 30 years with the development of nicotine chewing gum. This was followed by transdermal, nasal, and oral nicotine vapour inhalers. These Alternative Nicotine Delivery Systems (ANDS) were developed to decrease the craving of tobacco withdrawal and improve abstinence.

Many studies confirm the ability of these systems to improve 'quit rates' but their impact on long-term tobacco abstinence is modest.⁴ Generally, their pharmacokinetics are designed to provide low doses of nicotine over a prolonged period rather than the high-dose burst from smoking. Currently, the addicted smoker only has tobacco to provide this nicotine burst, and only gains access to alternative nicotine in the context of quitting smoking. Paradoxically, access to the safer forms of nicotine is often highly restricted, a point that has been previously emphasised.^{5,6} Indeed, the relationships between tobacco and nicotine (in the context of the public's health) have only recently been explored.⁷

Tobacco control

In the last 30 years, tobacco control strategies have considerably reduced smoking in some countries. The most successful have employed multiple approaches, including mandatory packet warnings, price increases, a ban on tobacco advertising, smoke-free environment legislation, health education, the provision of quit programmes, and litigation against the tobacco industry.

New Zealand has employed all of these strategies and, between 1970 and 2001, per-capita tobacco consumption has reduced by 60%. Adult smoking prevalence has decreased from 36% in 1976 to 28% in 1990. But since the 1990s, smoking prevalence has remained static. For Maori adults, the reductions have been much less dramatic (from 58% in 1976 to 51% in 2001). Furthermore, for Pacific Island adults, there has been an even smaller decrease (from 35% to 31%).

Nowadays, socioeconomic disparity is even greater, with smoking prevalence three-fold higher for those from families with annual incomes below \$20,000 compared to those with annual incomes above \$120,000.⁸ In New Zealand, the decline in smoking prevalence has stalled, and for Maori and Pacific people has been negligible. This socioeconomic and ethnic disparity in smoking prevalence clearly illustrates that in New Zealand, at least, tobacco control has largely benefited the more affluent. In fact, smoking prevalence amongst the poorest members of New Zealand's society was higher in 2001 than the overall smoking prevalence in 1976.

Such disparity is evident elsewhere, for example in the UK, where a similar three-fold disparity in smoking prevalence exists between the most and least advantaged groups.⁹ In the UK, this disparity is beginning to be recognised for the targeting of smoking cessation services (with some evidence of benefit).¹⁰

Perversely, the very success of tobacco control has left the remaining smokers and most of the world's developing economies in the unfettered embrace of a demonised tobacco industry. The outrage from public health at the tobacco industry's intransigence and tactics has clouded the entirely separate issues of tobacco and nicotine, rendering the idea of developing recreational or long-term replacement nicotine, a heresy. The introduction of alternative forms of nicotine as abstinence-promoting therapies have been tightly regulated, initially by prescription and latterly by restriction to pharmacies. The fundamental flaw has been the failure to separate nicotine from tobacco, both literally and metaphorically.

New approaches to nicotine replacement are required as Bates has suggested.¹¹ There are now a large number of Alternative Nicotine Delivery Systems available. A first step would be to make them as widely available as tobacco and significantly cheaper. Specifically, nicotine needs to be taken out of the pharmacy to openly compete with tobacco at every outlet. Moreover, the role of ANDS needs to be redefined—from improving abstinence rates to long-term replacement for tobacco for those smokers unable (or unwilling) to quit.

Studies of ANDS as long-term replacement will be required to define the most useful therapies singly and in combination—particularly among low-income and marginalised groups. However to implement a comprehensive nicotine replacement strategy, an effective inhaled nicotine delivery system (designed to deliver cigarette-like doses safely) will be needed.

Inhaled nicotine

Since the development of the metered dose inhaler in the 1960s, the pharmaceutical industry has gradually refined and improved the pulmonary delivery of drugs, principally for the management of asthma. The recent need to reformulate asthma treatments (such as beclomethasone) as liquids rather than solid particles in CFC-free carriers has led to smaller particle sizes and a doubling of potency (12). The goal of these therapies is to provide high doses locally at the airway mucosa. The aim of pulmonary nicotine delivery will be to deliver nicotine to the brain via the lung. Such inhaled nicotine delivery systems are not without risk.

First, a focus on them may distract policy-makers and the health-promotion workforce from other aspects of ongoing comprehensive tobacco control. Second, nicotine itself is not without adverse health effect, although (without doubt) nicotine is much less

dangerous to health than tobacco. Third, the availability of high-dose nicotine may dissuade people from quitting, and encourage initiation of a new nicotine habit among youth who would not have commenced smoking tobacco otherwise.

Several key elements would need to accompany any serious programme to introduce inhaled nicotine, however the devices and their effects must be acceptable to smokers. Specifically, they must be able to approximate the nicotine bolus obtained from smoking, and there would be an inevitable trade-off between sufficient appeal to smokers and insufficient appeal to experimental adolescents.

Nicotine at some mucosal surfaces is painful. As the tobacco industry was well aware of this early on, it introduced mentholated cigarettes (menthol being a weak local anaesthetic) to ease neophytes into their addiction. The development and marketing of inhaled nicotine would require close cooperation between state and enterprise to ensure a balance with tobacco abstinence strategies. The financial and legislative barriers to developing, and then marketing, the appropriate technology are considerable. Without support, and a carefully crafted strategic approach from governments, public health, and the anti-tobacco lobbies, the risks for any industry far outweigh the benefits. But in an appropriate regulatory climate, in which a long-term strategy for marketing had been agreed, there could be sufficient incentives for development of inhaled nicotine and extension of nicotine-delivery programmes.

New Zealand has some characteristics that make it an ideal country to pioneer such an approach. New Zealand has a strong long-standing commitment to public health and has pioneered smoke-free legislation, mechanisms to control tobacco, and the provision of alternative forms of nicotine. Despite these efforts, continuing reductions in smoking prevalence have slowed considerably and have largely benefited the more affluent sectors of society. Regarding extended nicotine programmes, New Zealand is a small isolated country separated by thousands of kilometres of ocean in all directions frustrating smuggling and a black market in tobacco. There are also precedents for partnerships between government and the pharmaceutical industry.

For example, the New Zealand government is currently investing \$200 million developing a vaccine for hyperendemic meningococcal disease. Meningococcaemia kills approximately 20 people per year in New Zealand, whereas tobacco kills close to 5000 per year. Currently, the New Zealand government collects \$880 million of revenue from tobacco annually. A small proportion of this revenue could be used to help develop a comprehensive nicotine-replacement programme.

There is an urgent need for new approaches to tobacco. The failure to separate tobacco from nicotine is a major barrier to further progress in preventing tobacco-related disease. Once separated, there is every reason to expect that, with an appropriate mix of incentive and regulation, a replacement nicotine strategy (including inhaled forms), could be developed and successfully introduced.

Governments need to be reassured that it will be considerably less harmful than tobacco and that recruitment to a new addiction industry is minimised. Regular monitoring will be required. Industry must be satisfied that it is financially viable and that there is an appropriate legislative framework in place to allow effective market entry. Essentially 'Big Pharma' needs to compete with 'Big Tobacco'. Most importantly, it must satisfy the addicted smoker who will need to be encouraged to switch from tobacco to nicotine with a mixture of marketing and financial incentives.

Furthermore, it must be readily available, and sit in a new niche between recreation and therapy. Once established and acceptable, tobacco as a nicotine delivery system will gradually disappear, and with it the whole issue of environmental tobacco-smoke exposure. None of this is likely to be easy, but neither is it impossible, and the potential gains are enormous.

The use of tobacco is part of almost every culture, and despite the best efforts of health professionals and regulatory authorities over the last 30–40 years, it is still readily available in every country and used by approximately one sixth of the World's population. In New Zealand, tobacco control has taken us a considerable way down the road to smoking abstinence, but the reductions have been inequitable and have lost momentum. While we need to retain many of the current tobacco control strategies, we urgently need new approaches and one of these is alternative nicotine replacement.

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