

Tobacco, nicotine and harm reduction

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Abstract

Issues. Tobacco smoking, sustained by nicotine dependence, is a chronic relapsing disorder, which in many cases results in lifelong cigarette use and consequent death of one out of two lifelong smokers from a disease caused by their smoking. Most toxicity due to cigarette smoking is related to the burning process. **Approach.** Models of harm reduction applied to tobacco suggest that use of non-combustible, less toxic, nicotine-containing products as a substitute for cigarette smoking would reduce the death toll arising from tobacco use. Available options include medicinal nicotine and smokeless tobacco products. **Key Findings.** The potential role of nicotine replacement therapy (NRT) products in a harm reduction strategy is currently severely restricted by strict regulations on dose, safety and potential addictiveness. As a result, NRT products are designed to provide much less nicotine, and deliver it to the brain more slowly, than cigarettes, which are widely accessible and poorly regulated. Smokeless tobacco (snus) has proved to be an acceptable reduced hazard alternative to smoking in Sweden, but supply of snus is illegal elsewhere in the European Union. **Implications.** To increase accessibility and reach more smokers, barriers to the use of NRT use need to be removed and more effective NRTs need urgently to be developed. Smokeless tobacco could also play an important role in harm reduction, but current European Union regulations and concerns over exploitation by tobacco companies currently preclude wider use. **Conclusion.** To improve public health there is an urgent need for an appropriate regulatory framework and regulatory authority at the European level, controlling both tobacco and nicotine products to ensure that the least harmful products are the most accessible. [Le Houezec J, McNeill A, Britton J. Tobacco, nicotine and harm reduction. *Drug Alcohol Rev* 2011;30:119–123]

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Tobacco smoking is a chronic relapsing mental disorder

Tobacco smoking, sustained by nicotine dependence, is classified as a chronic relapsing mental disorder [1,2] that for most users entails a struggle to achieve long-term abstinence. Current smoking cessation best practice involves the delivery of behavioural support in conjunction with pharmacotherapy [3,4]. The overall efficacy of these interventions is relatively low however, with at best approximately 20% of smokers typically achieving cessation at 1 year. The proportion of smokers using cessation services is also very low. For example, in Great Britain, where national networks of cessation services available to all smokers have been established, it is estimated that approximately 9% of current smokers had been referred or had self-referred to such a service in 2007 [5]. In practice, most smokers

try to quit by themselves, without support, which is the least effective method (rate of success of 1–3%) [6]. It is therefore important to find methods of improving the efficacy and the acceptability and uptake of cessation support. However, given the difficulties in quitting and the harm caused by continued smoking, it is also important that efforts are made to reduce the harmfulness of those who cannot, or do not want to, stop.

Most of the harm is caused by smoking, not nicotine

Tobacco smoking is the largest single preventable cause of many chronic diseases, including cancers, pulmonary and cardiovascular diseases, and currently causes around 730 000 deaths in the European Union (EU) each year (including 80 000 from passive smoking) [7]. In Europe, as in many parts of the world, tobacco use is

dominated by cigarette smoking. Cigarettes are the most deadly smoked tobacco product, because most toxicity is related to the burning process, and the health hazards of cigarette smoking are well known [8]. Smoke is harmful (the combustion of any plant produces toxic substances, such as carcinogens, carbon monoxide or oxidant gases), and smoking is the most addictive route of administration for a drug (e.g. crack vs. cocaine) because it delivers high doses of the drug very quickly to the brain [9,10].

Nicotine is considered to be the major substance responsible for tobacco dependence. Nicotine is not completely harmless, but it is not responsible for most of the diseases due to tobacco use. Unfortunately, over the years, nicotine has been associated with tobacco-related diseases in many media campaigns against smoking. Because of this, there are strong barriers to the use of nicotine for treatment of tobacco dependence, coming not only from tobacco users, but also from the medical community [11,12].

Models of harm reduction applied to tobacco suggest that the use of non-combustible, less toxic, nicotine-containing products would be better than cigarette smoking in limiting the death toll. Nicotine replacement therapy (NRT) is generally regarded as safe other than when used in pregnancy where the evidence is limited [10]. Although there is little evidence on long-term use of NRT, it is thought to be unlikely that there would be major long-term adverse effects on health, and certainly not in relation to the hazards of smoking. Smokeless tobacco products (STPs) are not a homogeneous category and the risk profile varies according to the products [10]. Evidence of the key risks to health from STPs is summarised in the next section.

Health risks of STPs

Respiratory diseases, predominantly lung cancer, chronic obstructive pulmonary disease and pneumonia, account for 46% of the deaths caused by cigarette smoking in the EU [7]. There is no evidence that STPs cause any of these major respiratory diseases. If smoked tobacco were completely replaced by STPs therefore, nearly half of all deaths caused by smoking might be prevented. In addition, as STPs do not produce smoke, they will not cause any of the health problems linked to passive smoke exposure in adults or children.

Other risks of STPs vary between the different products available [13]. Both animal experiments and epidemiological studies indicate that oral tobacco use has short-term effects on blood pressure and heart rate. Whether long-term use increases the risk of hypertension is uncertain. Although three large cohort studies have reported a statistically significant effect of STP on myocardial infarction, the evidence on snus and myo-

cardial infarction is more mixed with only one out of six studies in long-term Swedish snus users finding an increased risk of snus over never tobacco users [10]. STPs vary widely in terms of content in carcinogenic compounds [13]. Some products also contain other substances (e.g. areca nut) that may also be carcinogenic, which makes difficult to disentangle these effects from those of tobacco itself [14]. The use of STPs, including snus, appears to be associated with an increased risk of pancreatic cancer, although to a lesser extent than the use of smoked tobacco. It also appears that the risk of oral cancer associated with the use of STPs with low levels of nitrosamines, such as snus, is small or non-existent [14].

Overall however, and with the exception of use in pregnancy, use of STPs and particularly snus are clearly substantially less hazardous than cigarette smoking [13]. This conclusion is also reached by the only systematic review of the evidence from studies that allow direct comparison of relative risks of smoking and smokeless in the same populations [15]. The magnitude of the overall reduction in hazard is difficult to estimate, but is at least 50% for cardiovascular disease, at least 30% for pancreatic cancer, at least 50% and probably more for oral and other gastrointestinal cancer, and possibly 100% for lung cancer and chronic obstructive pulmonary disease [13]. A recent study using a modified Delphi approach (judgement by a panel of experts) to estimate the relative hazard of snus concluded that the product was likely to be approximately 90% less harmful than smoking [16].

Harm reduction in tobacco use

To date, tobacco control policy has mostly focused on two principles: (i) that young people should not start smoking and (ii) that current smokers should quit. Harm reduction approaches have largely been focused on reducing the harmfulness of exposure to second-hand smoke. However, many smokers cannot or do not want to give up, and little effort has been put into reducing the harmfulness of their continued tobacco use. Tobacco harm reduction is the lessening of the net damage to health associated with the use of tobacco products. Smoking usually starts in adolescence and determination to quit probably peaks in middle age, typically at 35–50 years of age. This can result in a successful quit attempt where harm can be reduced to that of a never-smoker depending on the age at which cessation occurs [8]. Continued cigarette smoking will cause the maximum harm, so a reduction in harm will result from any action that decreases the risk from continuing smoking. The sooner the action starts and the less hazardous the product is, the greater the harm reduction [17].

The tobacco industry has developed potentially reduced exposure products, which deliver smoke containing lower levels of nitrosamines or other toxins. However, none of these products has been shown appreciably to reduce the health hazard of tobacco use, and it is perhaps unlikely that any product that involves inhalation of products of combustion will ever present as low a hazard as smokeless tobacco or medicinal nicotine alternatives. There is, however, a much broader spectrum of risk associated with these alternative nicotine products, in which smoked tobacco represents one extreme, and medicinal nicotine (NRT) the other [18]. Switching smokers from inhalation of the combustion products of tobacco in any form to a non-combustible nicotine delivery product would likely result in a vast reduction in tobacco-caused death and illness, via major reductions in lung cancer and chronic respiratory disorders. However, there are a number of obstacles to this route, many of them arising from the regulatory systems that currently govern the use of nicotine products in our society.

Nicotine replacement therapy products are currently produced and marketed as medicinal products for use as cessation aids, not as a longer-term substitute for cigarette smoking. The ideal NRT product would be one that provides nicotine in a dose and rate that satisfies the craving and other withdrawal effects experienced by the smoker, without the harmful components of cigarette smoke. The medicinal NRT products currently available have achieved only partial success with regard to these issues, in particular tending to provide nicotine at doses and rates of delivery that are a poor substitute for cigarettes [19]. This has been done largely because of risk adverse medicines regulatory frameworks, which compare the use of NRT against placebo rather than against continued smoking. In addition, NRT products are available through fewer retail outlets than cigarettes and their medicinal packaging and pricing means that they are less appealing to tobacco users than cigarettes. The regulation of NRT has recently been changed, and is more relaxed in some countries (e.g. France, UK), but if we want NRT to compete against tobacco efficiently we need to improve this situation and make NRT much more accessible, and much more affordable than cigarettes. It is also important to encourage the development of more effective NRTs. In its recently published report, *Action on Smoking and Health in England* focused on some of the steps needed to achieve this [20].

There is also potential for harm reduction by use of STPs. Snus is an example of a reduced harm product that is widely recognised to have contributed to reductions in tobacco-attributable mortality and oral cancer incidence rates in Sweden, and thus to reduce the net harm to health from tobacco use [21]. Although there is

a concern that the availability of lower hazard tobacco products, marketed by tobacco companies, may lead to use among people who would not otherwise have used a tobacco product, at low levels of hazard, any public health impact from this is likely to be more than offset if substantial numbers of smokers switch to the lower hazard product [22,23]. However, there is disagreement on the extent to which snus has contributed to declining smoking prevalence in Sweden, and whether this experience and the balance of harm to benefit to society arising from the availability of snus could be replicated in other countries [13]. Currently, supplying snus is illegal in EU countries other than Sweden.

The ideal option, aside from quitting all nicotine use, would be for smokers to switch from cigarettes to a 'clean addictive nicotine delivery system' [24]; an idea that is now gaining increasing support. However, the development of such products is unlikely in the context of the regulatory systems that currently pertain across Europe.

Nicotine product regulation in the EU

The EU currently regulates nicotine products in a piecemeal and grossly inconsistent manner. Medicinal NRT products are controlled under drug regulations, and subject to strict controls on purity, promotion, prescription, and on the evidence base needed for licensing. Cigarettes, on the other hand, are subject to restrictions on advertising, printing of health warnings on packs and in some countries on use in enclosed places, but the product itself is unregulated. Some STPs, which in terms of hazard fall somewhere between the two extremes above, are subject to even more extreme and inconsistent regulation; products intended to be used by chewing or sniffing are widely accessible and virtually unregulated [25], while products that are intended to be sucked (including snus) are banned under EU directive 2001/37/EC2 [26]. Sweden alone is exempt from this directive.

This lack of regulatory consistency creates a strange situation in which smokers' choice of nicotine product is restricted, and smoked forms continue to be favoured over non-combustible nicotine delivery systems. This system clearly works against public health. If the development of new and improved nicotine delivery systems is to be encouraged in the future, it is imperative to have a clear regulatory framework within which all nicotine products can be assessed in relation to their health impact. The aim of such a framework should be to reduce the health effects of tobacco use by minimising the use of nicotine-containing products overall, but among regular users to maximise the use of safer nicotine products and minimise the use of combustible products. The ban on sucked tobacco products was

enacted amid concerns about introducing youth to tobacco. At that time, there were minimal restrictions on tobacco advertising and promotion and while many EU countries now have comprehensive bans on promotion, there are still concerns that the tobacco industry exploits loopholes to promote their products. Having access to a comprehensive surveillance system would be critical in order to be able to respond quickly to any untoward changes in nicotine use [10]. In its second report on the implementation of the 2001 Product Directive, the Commission commented that it would study the regulatory challenges with a view to at least ensuring that new tobacco and/or nicotine products marketed are regulated properly at EC level to serve the public health and internal market objectives. The Commission will also look at the relationship of the tobacco products regulatory framework with the novel foods and pharmaceutical legislation. We look forward to the outcome of this review [27].

New regulatory framework: the need for a nicotine and tobacco regulatory body

The prevention of smoking-related diseases has entered a new phase. Many countries have ratified the World Health Organization's Framework Convention on Tobacco Control, which came into effect on 27 February 2005. Countries signing up to the agreement committed themselves to introducing new governance that would enable them to implement various actions in the most effective way. The EU is also proposing to reinforce national policies on tobacco control. This context should encourage new thinking about tobacco and nicotine regulation and should favour taking tobacco and medicinal nicotine out of their existing regulatory frameworks and into a new structure.

Creating a new institution to manage regulation has been the approach favoured in many countries for the regulation of drugs and food, and has been the preferred approach at least in Ireland and Norway for tobacco regulation. Establishing a single institution with a combined remit of tobacco and nicotine regulation would probably be the most efficient and coordinated way to enable a comprehensive approach to co-regulate nicotine and tobacco products. A new institution would mean that a permanently staffed agency would be created with adequate authority to create an appropriate regulatory framework for tobacco and nicotine [10]. The Royal College of Physicians, in the UK, believes that developing a new institution is the optimum approach to nicotine and tobacco products commensurate with the scale of the problem and the complexities of the regulatory responses needed [10,14]. In France, the Comité National Contre le Tabagisme (National Committee Against Tobacco Use) and the Ligue Nationale Contre le

Cancer (French Cancer League) have expressed a similar position, and have recommended the creation of a tobacco and nicotine regulatory authority (<http://www.cnct.fr/tous-les-dossiers-73/plaider-pour-la-mise-en-place-d-une-autorite-nationale-francaise-1-19>). This regulatory body should work with other national organisations across Europe, which are either in the process of being set up or already established as in Ireland and Norway. It would be responsible for formulating decisions about how tobacco and nicotine products will be regulated and overall responsibility for tobacco control [28]. An outline of the major duties and responsibilities of such an authority working at national level has been published in the UK [14].

Conclusions

As reflected by the recent smoke-free and other tobacco control policies established in many European countries, tobacco control has greatly progressed over the last decade. However, efficient control over tobacco use would mean that we take every possible step to improve public health. An urgent one would be to regulate tobacco and nicotine products in relation to their respective harmfulness in order to progressively eliminate the most harmful products and convince the smokers who cannot stop all tobacco use to switch to less harmful nicotine sources. This would also have an impact on youth smoking as these measures will participate to the denormalisation of tobacco use as is the case with smoke-free policies.

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References

- [1] American Psychiatric Association. Diagnostic and statistical manual of mental disorders, 4th edn. Washington, DC: American Psychiatric Association, 1994.
- [2] World Health Organization. International Classification of Diseases, 10th Revision (ICD-10). Geneva: World Health Organization, 1992.
- [3] West R, McNeill A, Raw M. Smoking cessation guidelines for health professionals: an update. *Thorax* 2000;55:987-99.
- [4] Fiore MC, Jaen CR, Baker TB, *et al.* Treating tobacco use and dependence: 2008 update. Rockville, MD: USDHHS, U.S. Public Health Service, 2008.
- [5] Lader D. Smoking-related behaviour and attitudes, 2007. Office for National Statistics. Omnibus Survey; Wales, 2008. Available at: http://www.statistics.gov.uk/downloads/theme_health/smoking2007.pdf (accessed 15 Nov 2010).
- [6] Hughes JR. Motivating and helping smokers to stop smoking. *J Gen Intern Med* 2003;18:1053-7.

- [7] ASPECT Consortium. Tobacco or health in the European Union. Luxembourg: European Commission, 2004.
- [8] Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. *Br Med J* 2004;328:1519–28.
- [9] Le Houezec J. Role of nicotine pharmacokinetics in nicotine addiction and nicotine replacement therapy: a review. *Int J Tuberc Lung Dis* 2003;7:811–19.
- [10] Royal College of Physicians. Harm reduction in nicotine addiction. London: Royal College of Physicians, 2007.
- [11] Cummings KM, Hyland A, Giovino GA, Hastrup JL, Bauer JE, Bansal MA. Are smokers adequately informed about the health risks of smoking and medicinal nicotine? *Nicotine Tob Res* 2004;6(Suppl. 3):S333–40.
- [12] Siahpush M, McNeill A, Borland R, Fong G. Socioeconomic variations in nicotine dependence, self-efficacy and intention to quit across four countries: findings from the international tobacco control policy evaluation survey. *Tob Control* 2006;15(Suppl. 3):iii71–5.
- [13] SCENIHR (Scientific Committee on Emerging and Newly-Identified Health Risks). Scientific opinion on the health effects of smokeless tobacco products. 6 February 2008. Available at: http://ec.europa.eu/health/scientific_committees/consultations/public_consultations/scenihr_cons_06_en.htm (accessed 15 Nov 2010).
- [14] Royal College of Physicians. Ending tobacco smoking in Britain. Radical strategies for prevention and harm reduction in nicotine addiction. London: Royal College of Physicians, 2008. Available at: <http://bookshop.rcplondon.ac.uk/details.aspx?e=259> (accessed 15 Nov 2010).
- [15] Roth DH, Roth AB, Liu X. Health risks of smoking compared to Swedish snus. *Inhal Toxicol* 2005;17:741–8.
- [16] Levy DT, Mumford EA, Cummings KM, *et al.* The relative risks of a low-nitrosamine smokeless tobacco product compared with smoking cigarettes: estimates of a panel of experts. *Cancer Epidemiol Biomarkers Prev* 2004;13:2035–42.
- [17] Martinet Y, Bohadana A, Fagerström K. Would alternate tobacco products use be better than smoking. *Lung Cancer* 2006;53:1–4.
- [18] European Respiratory Society. Tobacco smoking: harm reduction strategies. An ERS research seminar. Brussels: ERSJ Ltd, 2006.
- [19] Henningfield JE. Drug therapy: nicotine medications for smoking cessation. *N Engl J Med* 1995;333:1196–203.
- [20] Action on Smoking and Health. Beyond smoking kills: protecting children, reducing inequalities. London: ASH, 2008. Available at: <http://www.ash.org.uk/beyondsmokingkills> (accessed 15 Nov 2010).
- [21] Swedish National Board of Health and Welfare. Folkhalsorapport 2005. Stockholm: Socialstyrelsen, 2005.
- [22] Foulds J, Kozlowski L. Snus—what should the public-health response be? *Lancet* 2007;369:1976–8.
- [23] Gartner CE, Hall WD, Vos T, Bertram MY, Wallace AL, Lim SS. Assessment of Swedish snus for tobacco harm reduction: an epidemiological modelling study. *Lancet* 2007;369:2010–14.
- [24] Gray N, Boyle P. The future of the nicotine-addiction market. *Lancet* 2003;362:845–6.
- [25] Longman J, Pritchard C, McNeill A, Csikar J, Croucher R. Accessibility of chewing tobacco products in England. *J Public Health (Oxf)* 2010;32:372–8.
- [26] Directive 2001/37/EC of the European Parliament and of the Council of 5 June 2001 on the approximation of the laws, regulations and administrative provisions of the Member States concerning the manufacture, presentation and sale of tobacco products. Official Journal L 194, 18/07/2001:0026–0035 [EURLEX].
- [27] European Commission. Report from the Commission to the European Parliament, the Council and the European Economic and Social Committee. Second report on the application of the tobacco products directive. 2007. Available at: http://ec.europa.eu/health/ph_determinants/life_style/Tobacco/Documents/tobacco_products_en.pdf (accessed 15 Nov 2010).
- [28] Le Houezec J, Hirsch A, Martinet Y. Letter: time for a tobacco and nicotine regulatory authority for France. *Tob Control* 2006;15:343–4.