

12

Smoking cessation and nicotine-replacement therapies

*Thomas E. Novotny, Jillian Clare Cohen, Ayda Yurekli,
David Sweanor, and Joy de Beyer*

Initiatives that help smokers to quit are key components in an effective tobacco-control program. Unaided, individuals' chances of quitting are low, but success rates are higher when smokers use nicotine-replacement therapies (NRTs) and other pharmacological therapies. The current market for NRTs worldwide is small compared with the market for cigarettes, and is mostly concentrated in high-income countries. The small market largely reflects low levels of demand, especially in low-income and middle-income countries. However, the regulation of NRTs, for example through conditions of sale, also reduces access to them. Public policy options for increasing access to NRTs include the deregulation of conditions of sale. In addition, increased public information about the hazards of smoking and the benefits of cessation appear to be important for increasing demand for NRTs. Where studied, NRTs have been found to be cost-effective. Theoretically, these therapies could be publicly financed for the poorest smokers. In practice, however, it would be difficult to target those on the lowest incomes.

12.1 Introduction

Support for smoking cessation is an important component of comprehensive population-based tobacco-control programs (Novotny *et al.* 1992). Given current patterns of smoking, 100 million adults who currently smoke will be killed prematurely by tobacco over the next 20 years (Peto *et al.* 1999). Smokers who quit before the onset of major illnesses, especially those who quit at earlier ages, avoid most of the excess risk accrued by continuing smokers (Doll *et al.* 1994). The benefits of quitting have been extensively documented and include reduction of risk for all major forms of tobacco-attributable disease and improved life expectancy (Chapter 2; USDHHS 1990).

This chapter reviews cessation methods, focusing on nicotine-replacement therapy (NRT), and, to a lesser extent, on other pharmacological adjuncts to cessation, such as bupropion. The chapter has three parts. First, we review briefly the effectiveness of various types of cessation. (More details of cessation methods can be found elsewhere: Fiore *et al.* 1996; USDHHS 1988, 1990; American Psychiatric Association 1996). Second, we discuss issues concerning the price of NRTs, public information about them, and regulations on their sale. Because NRT markets can only be understood in the context of the cigarette market, we compare the two products. Third, we explore

public policy options, including deregulation of NRT products and conditions of sale, and public or insurance financing for NRT.

12.2 Smoking cessation

In countries where there is relatively widespread knowledge about the risks of smoking and the benefits of quitting, a significant proportion of smokers will try to stop smoking each year. In the United States, for example, an estimated 16 million current daily smokers in 1997 had stopped smoking at least one day during the preceding year (US Centers for Disease Control and Prevention 1999a). Widespread quitting has contributed to reduced levels of lung cancer and cardiovascular disease in males in several high-income countries (Chapter 2).

Quitting smoking is well described by a 'stages of change' model (Prochaska and DiClemente 1983). According to this model, smokers move along a continuum of behavior, from pre-contemplation (not thinking of quitting), to contemplation (preparing to quit), action (cessation), and finally maintenance. Many factors may influence movement along this continuum. Kenkel and Chen (Chapter 8) and Saffer (Chapter 9) expand, respectively, on the effectiveness in reducing tobacco consumption of widespread public information about the risks of smoking and bans on advertising and promotion. Information will move some smokers from pre-contemplation to contemplation of quitting. Advertising and promotion bans may reduce the environmental cues that support smoking. Similarly, higher taxes may encourage some smokers to try quitting, as discussed by Chaloupka *et al.* (Chapter 10). The availability of effective cessation therapy might also help move smokers from pre-contemplation and contemplation stages to action and maintenance.

The success of unaided smoking cessation is low in relative terms, although it is the most common method used. Unaided cessation is common enough to have contributed to the accumulation, over time, of substantial numbers of male smokers quitting in high-income countries (USDHHS 1990). However, even where there is a high level of public awareness of the health dangers of smoking, only 3–5% of all smokers who try to quit by themselves are permanently successful on any given attempt. We summarize the effectiveness of three types of interventions that could increase the proportion of smokers who succeed in quitting: community cessation programs; specific advice from a health provider; and NRT or adjunct non-NRT pharmacological treatment. Most studies of efficacy for these interventions have been performed in high-income countries. Wherever possible, we discuss the applicability of these approaches to low-income and middle-income countries.

12.2.1 Community cessation programs

Community or population-based smoking-cessation projects aim to increase the number of quitters in a given community. These projects involve mass communications to raise public awareness, encouragement of health professionals to improve their efforts with individual patients, widespread provision of self-help materials through medical and non-medical channels, and smoking cessation events such as 'Quit and Win' contests (Foulds 1996). Some of these programs in the United States, notably in

California and Massachusetts, have been financed through a specific, one-time increase in cigarette tax (Bal *et al.* 1990). Few have used subsidies for cessation therapy.

Large-scale community cessation efforts in high-income countries have shown modest efficacy at best (Foulds 1996). In the United States, the Community Intervention Trial for Smoking Cessation (COMMIT) was a randomized controlled trial over 4 years that focused on quitting among heavy smokers in large communities (defined as those with populations between 50 000 and 250 000). This intervention included public information, interventions by health professionals, work-site activities, and the development of community cessation resources. There were no differences in quit rates for heavy smokers between the control and intervention communities, and there was only a 3% improvement in quitting among light-moderate smokers (COMMIT Research Group 1995). Somewhat more encouraging results were noted in the North Karelia project in Finland. In this non-randomized, community-based cardiovascular disease prevention program, the percentage of men currently smoking declined during the first 10 years of the program (from 50% to 37%), and this decline was sustained over the next 10 years (Vartiainen *et al.* 1998). This study found that 50% of those who could not stop smoking indicated a desire to do so. The authors suggested that NRT availability might improve the success of a community-based strategy. In the Netherlands, a non-randomized smoking cessation campaign involving the mass media included television shows, a television clinic, a quit line, local group programs, and a publicity campaign (Mudde and De Vries 1999). It produced high levels of program awareness and the number of smokers who abstained for a significant period increased by 4.5% over and above the baseline level. This success was probably reduced by a massive rise in tobacco promotion during the campaign. The cost per long-term quitter was \$12.

Well-evaluated community approaches to smoking cessation are rare in low-income or middle-income countries. Gupta *et al.* (1986) conducted a non-randomized trial among 36 471 tobacco smokers and chewers in three rural districts of India. Interventions included health professionals' advice, information campaigns in the mass media, and cessation camps. At the end of 5 years, the quit rates ranged from 9% to 17% in the intervention cohorts, and from 3% to 9% in the control cohorts, with the difference being statistically significant in two districts. However, community cessation programs are not likely to yield high *absolute* numbers of quitters in low-income and middle-income countries because, at present, these countries have lower overall quitting rates than high-income countries (Chapter 2). Also, some components of cessation programs in high-income countries (such as telephone help-lines) are less feasible or affordable in low or middle-income countries.

12.2.2 Advice from health providers

In many high-income countries, effective cessation treatment protocols are widely available to individual smokers as part of a medical approach. The US Agency for Health Care Policy and Research (AHCPR) published a thorough review of the literature and a discussion of these guidelines (Fiore *et al.* 1996). Briefly, the recommendations include screening all patients for tobacco use, advising patients who use tobacco to quit, setting a specific quit date, and providing NRTs. These treatments

include minimal counseling by health providers, brief or more extensive counseling by specially trained providers, and group-intensive counseling. All interventions will be more effective against a social milieu in which tobacco cessation and non-smoking are the norm (Novotny 1988). The AHCPR guidelines also call for infrastructure changes and reimbursement as ways to increase the availability and accessibility of treatment services and products.

Health providers can enhance individual cessation efforts through social support and other proactive interventions (Orleans *et al.* 1991). Individual or group counseling increases cessation rates substantially, but this approach also requires motivation for smokers to participate. Further disadvantages include the direct costs, and the opportunity costs (such as lost work time). Anthonisen *et al.* (1994) showed that a combination of intensive, specialized care, NRTs, behavioral modification, and relapse prevention training achieved the highest rates of cessation success, with 35% of the intervention group succeeding versus 9% of the controls. However, this intervention was in a group of adults with early signs of lung disease. The program was resource-intensive, expensive, and not applicable to general populations. Even with such intensive therapy, 65% of smokers did not quit, and of those that did, 37% had relapsed within 5 years.

In the United Kingdom, trained pharmacists provide information and support for smokers who seek NRT; interventions provided through pharmacists have increased counseling and improved cessation rates (Sinclair *et al.* 1998). In developing countries, where there is extensive self-medication and use of pharmacists for medical advice (Kamat and Nichter 1998), pharmacists could play a valuable role by advising clients of the benefits of cessation.

Overall, medically-based cessation interventions are unlikely to be accessible to individual smokers in low-income and middle-income countries. Smokers are unlikely even to seek treatment from physicians. Moreover, we are not aware of any studies of the effectiveness or cost-effectiveness of cessation advice provided by healthcare providers in a developing country.

12.2.3 Non-NRT therapies

Mood, or affect, appears to influence the likelihood of addiction. Bupropion hydrochloride, a widely used anti-depressant, has recently been marketed in the United States and Canada as an effective smoking cessation treatment (Hurt *et al.* 1997). Bupropion is not an addictive drug and can be used for longer periods for maintenance in appropriate patients (Miller and Griffith 1983). Some consumers may prefer non-nicotine products, such as bupropion, as a way of helping to end their addiction. A randomized trial comparing NRT patches and bupropion reported that cigarette abstinence at 12 months was 16.4% in the NRT patch group, 30.3% in the bupropion group, and 35.5% in the group treated with NRT patch and bupropion combined (Jorenby *et al.* 1999). Data on the population-wide efficacy or cost-effectiveness of this drug are not yet available. More research is needed to show whether anti-depressants or similar therapies can increase cessation rates among smokers in low- and middle-income countries. The market for these non-NRT therapies has not been extensively studied.

12.2.4 Nicotine and nicotine-replacement therapy

Nicotine is the primary active ingredient in cigarettes that reinforces individual smoking behavior (USDHHS 1990). However, it is other constituents of tobacco, and not nicotine, that cause widespread mortality and morbidity. Tobacco use can be classified as a 'dependence' within the criteria of the International Classification of Diseases (WHO 1994). The criteria include *use despite damage, physical* and *psychological dependence*. Knowledge of the addictive nature of nicotine provides a rationale for substituting a less-harmful source of nicotine for cigarettes.

NRT products take a number of forms: gum, transdermal patch, nasal spray, oral inhaler, and tablet. All of these products have different levels of efficacy and variable rates of nicotine absorption, and they are most effective when the consumer also receives parallel cessation-counseling, but nevertheless are effective even without accessory behavioral therapy (Fiore *et al.* 1996).

A number of studies have demonstrated the efficacy, safety, and utility of NRT (Silagy *et al.* 1994; Cromwell *et al.* 1997; Shiffman *et al.* 1997; Shiffman *et al.* 1998). Of smokers who use a pharmacological aid, such as NRT, 10–30% are able to stop smoking for at least six months (Fiore *et al.* 1996). This represents a significant improvement over the success of self-help and brief advice from a physician. NRT, in fact, has been found consistently to double a smoker's chances of successful quitting with or without concomitant behavioral therapy (Fowler 1998; Raw *et al.* 1999). Table 12.1 summarizes the evidence.

NRT products are used primarily to quit smoking and effectively treat the symptoms of nicotine withdrawal and are not prescribed or recommended for any other purpose (Silagy 1994). Other issues to consider are the health implications of long-term use of NRT alone (Fagerstrom *et al.* 1997), and the implications of the mixed use of NRT and cigarettes. A recent review of the risks and benefits of NRT reported several significant pieces of evidence regarding these products (Benowitz 1998). If used appropriately, NRTs are comparatively safe products. They emit no tar or carbon monoxide, and they produce lower blood nicotine levels than cigarettes. The use of nicotine products in individuals who are tolerant is not likely to be associated with any acute behavioral toxicity.

Table 12.1 Effectiveness of various cessation interventions

Intervention and comparison	Increase in percentage of smokers abstaining for 6 months or more
Brief advice to stop (3 to 10 minutes) by clinician versus no advice.	2 to 3
Adding NRT to brief advice versus brief advice alone or brief advice plus placebo.	6
Intensive support (e.g., smokers' clinic) plus NRT versus intensive support or intensive support plus placebo.	8

Sources: Fiore *et al.* 1996; Raw *et al.* 1999.

Table 12.2 Annual smoking cessation among 50 million smokers in the United States: utilization, efficacy and impact of different cessation interventions

Intervention	Utilization (number of smokers using the method annually)	Efficacy (percentage sustained quitting at 6 months)	Impact (number of sustained successful quitters annually)
None	22 800 000	3	684 000
NRT by prescription, 1995	2 500 000	14	350 000
Over-the-counter NRT, 1996	6 300 000	14	882 000
Behavioral counseling	395 000	24	94 800

Source: Shiffman *et al.* 1997; Shiffman *et al.* 1998.

Some smokers may need long-term nicotine maintenance therapy, which these products can offer. Exposure to nicotine with NRT use is generally no greater than the exposure during cigarette smoking, and because NRT products do not contain the toxic chemicals found in cigarettes, the benefits of nicotine maintenance therapy almost certainly outweigh the risks of NRT. Use of nicotine in pregnancy may be associated with spontaneous abortion, low birthweight, and neonatal toxicity. NRT will certainly be less hazardous than cigarettes, but should only be used by pregnant women to completely cease cigarette smoking. Controlled clinical trials of NRT in smokers with documented cardiovascular disease have found no evidence that NRT products are harmful, even if used for as long as 5 years. Finally, limited data suggests that use of NRTs by smokers—for example, in non-smoking situations such as air travel or workplaces—reduces the overall amount of smoking, and thus confers health benefits. However, more research is required in this area.

Table 12.2 provides estimates of the population impact of cessation with or without NRT, based on data from the United States (Schiffman *et al.* 1997; Schiffman *et al.* 1998). The authors estimated that adding pharmacological therapy to other cessation methods could increase the quitting rate from 3% to 14%.

With increasing restrictions on smoking in workplaces and public transportation in most of the world (WHO 1997), demand for NRT products could increase. The availability of pharmacotherapy for nicotine-dependent smokers may even make it easier to implement health policies aimed at smoking cessation and establishing smoke-free environments because affected employees now have alternatives that could help them avoid nicotine withdrawal symptoms.

In sum, NRTs appear to be effective and feasible for use in high-income countries. We now describe the NRT market.

12.3 Key issues in the nicotine market

Currently, NRT products compete with large legal and illegal markets in cigarettes. In many countries, the cigarette industry is a duopoly or oligopoly. In India and some

other countries, however, there are also significant sales of other nicotine-containing products (snuff, chew, etc.) that are not controlled by the same companies. In order to understand how NRT and other pharmacological cessation products compete with the established nicotine market, it is important to understand some dynamics of this market. Key factors include: market size and relative market shares, product characteristics (including effectiveness), public information, and cost.

12.3.1 Market size and shares

NRT products represent only a tiny fraction (less than half of 1%) of the global pharmaceutical market, which was around \$300 billion in 1998 (*Script Magazine* 1999). The global market for NRT products was estimated to be only \$725 million in 1998, about \$553 million of which was in the United States. Nicotine gum accounts for almost half of this, with the patch second. In contrast, cigarettes comprise a world retail market of some US\$300 billion (WHO, 1999), more than 440 times larger than NRT sales. The future growth of the NRT market depends on several factors, some of which are discussed below.

In comparison with cigarettes, NRT products are much less widely available worldwide. Figures for NRT availability have been compiled by the Medical Information Database (MIDAS), which contains data on international and national pharmaceutical products, such as average ex-manufacturing price, average price for consumer, sales in US dollars, sales in terms of standard dose unit, and the number of sales packages (IMS Global Services 1998). MIDAS excludes some major European countries such as Denmark, Sweden, and Switzerland. MIDAS expenditure data for 1996 reveals that, of 63 countries assessed, NRT products were available in 21 high-income, 27 middle-income, and only 2 low-income countries. In most countries, patches account for over 95% of the NRT market. Almost 70% of global NRT product sales are in the United States, nearly 20% of sales are in Europe, and 10% in other industrialized countries. Middle-income countries have less than 1% of the NRT market share, while NRT sales are almost non-existent in low-income countries.

12.3.2 Product characteristics

Tobacco products are designed to encourage long-term nicotine maintenance with maximum consumer utility. They also deliver other products that are harmful to health. NRT products, on the other hand, are produced to assist nicotine-dependent smokers who want to quit. They provide users with a small amount of nicotine to reduce withdrawal symptoms. Tobacco products and NRT products are substantially different, not only in their components, but also in their effectiveness as nicotine delivery devices and the way in which they are sold. Table 12.3 summarizes these differences.

Smoking results in rapid peak nicotine levels. Nicotine from cigarettes is quickly absorbed via the lungs of smokers and reaches the brain within seconds. NRT products, on the other hand, are designed to deliver more gradual increases in blood levels of nicotine without the peaks and valleys associated with cigarettes. With nicotine gum, patches, and inhalers, nicotine is absorbed gradually through the mouth, skin, or respiratory passages (Schneider *et al.* 1996; Shiffman *et al.* 1998). Nicotine nasal spray provides a rather rapid absorption, and hence may be more like the dosing experience of smoking cigarettes.

Table 12.3 Differences between pharmaceutical NRT products and cigarettes

Pharmaceutical NRT products	Cigarettes
Subject to strict regulations including safety standards for use.	Limited regulatory control with no safety standards for use.
Lower abuse potential.	Maximize pleasurable/reinforcing effects of addiction.
Appeal and acceptability targeted to consumers for indicated use, minimizing youth appeal.	High sensory and packaging appeal targeted to susceptible youth.
Slow nicotine absorption rates.	Fast nicotine absorption rates.
Rigorous manufacturing standards.	Non-rigorous manufacturing standards.
Safe if used as intended.	Hazardous if used as intended; risks minimized by manufacturers.
Select distribution points.	Wide distribution networks.
May increase quit rates among smokers.	Significant population health risk.
Designed for short-term use and treatment of nicotine dependence.	Designed for long-term use, creation, and maintenance of nicotine dependence.
Costly in up-front costs, but comparable to cigarettes on daily cost.	Inexpensive, sold in small less costly units.

Source: Based on Warner *et al.* 1997, 1998.

12.3.3 Consumer information about NRT products

Compared with cigarettes, there have been only minor initiatives to inform consumers about NRT products or to market them. Moreover, NRT advertising campaigns have had a rather narrow focus, presenting a product for use by committed quitters and not acting as a cue to all smokers to quit. Although comprehensive global information on the regulation of advertising or distribution of NRT products is not available, the existing evidence suggests that many governments treat NRTs like other pharmaceutical products and prevent their manufacturers from advertising them directly to consumers. A few high-income countries are exceptions to this pattern.

Among the public, knowledge about NRT is poor, and misinformation about nicotine is widespread. Even health professionals commonly confuse the effects of nicotine with the effects of its main delivery vehicle, the cigarette. Surveys in several countries find that high percentages of the public, and of physicians, erroneously believe that nicotine itself causes cancer. For example, a survey of five high-income countries found that 43% of respondents believed that nicotine causes cancer and 33% were not sure.¹ In the United States, a 1997 survey of perceptions about the effects

¹ Based on unpublished survey data provided by Pharmacia and Upjohn 1996, 1997.

of tar and nicotine found that more than 80% of smokers mistakenly believed that the nicotine in cigarettes causes emphysema, cancer, and cardiovascular disease (Porter Novelli 1997). A recent Gallup poll confirmed that consumers do not understand the characteristics of nicotine, the benefits of NRT, or the risks of continuing to smoke so-called 'light' cigarettes. In this survey, 40% believed that NRT could cause or worsen health problems (Gallup Organization 1998). These findings indicate a clear need for better information about nicotine and NRTs for policy-makers, health professionals, and the public. Health providers trained in the use of NRT and in protocols to assist smokers could be a useful additional source of information to their patients.

Better publicity about NRTs may motivate quit attempts among smokers who would not have otherwise tried. Within the Prochaska model of stages of quitting, it is reasoned that smokers may move along the continuum of quitting, from contemplation to action, if they have access to both information about NRT products and the products themselves. A recent poll in the United States found that about 30% of current smokers were more motivated to think about quitting, or would actually quit smoking, if NRT products or other proven treatments were more readily available (Gallup Organization 1998). It is not clear whether this is a result of NRT advertising or due to the better availability of the NRT products. However, the survey reported that a large majority (86% of smokers and 89% of former smokers) felt that clinically proven cessation treatment should be as readily available as cigarettes.

12.3.4 Regulation

There are three broad and overlapping categories of consumer regulation (Room 1997) with respect to nicotine-containing products. We outline these, contrasting NRTs with cigarettes.

Regulation of the product

Tobacco products are not generally regulated in terms of health or manufacturing standards. Labeling for tar and nicotine content is required in only 36 countries (WHO 1997). Trade in tobacco products is less strictly regulated than NRT (see Chapter 14). On the other hand, NRT products are classified as pharmaceuticals, and must undergo various phases of approval in many countries before they are able to enter into a market. For example, a new drug requires a license, which is only granted after the product has had clinical trials and has been tested for safety, quality, and veracity and completeness of packaging information.

Modifications in cigarettes (e.g. toward lower tar levels) are permitted without regulation. In contrast, if a pharmaceutical company decides to modify a previously approved NRT product, it is obliged to seek further approval from the relevant regulatory authority. If a product is approved for consumption in one market, it must pass again through regulatory procedures if it is to enter another market.

Regulation of the provider or seller or the conditions of sale

In some countries, a license is required to sell tobacco, but throughout the developing world, tobacco is widely sold by small, unlicensed vendors. Like other pharmaceuticals, NRT products are generally sold only in pharmacies, either over the counter (OTC) or on prescription only. The exceptions are OTC NRT products in the United States, which may also be sold in grocery and general stores, and in the United Kingdom and Canada, where general retailers may also sell nicotine patches. These regulations would be difficult to enforce in many developing countries, where most pharmaceuticals are widely sold by vendors who are not pharmacists, with or without prescriptions, and few pharmacies have trained pharmacists in attendance. But to the extent that NRT products are sold only in pharmacies, the supply of physicians, pharmacies and pharmacists, and other bottlenecks in the distribution system, will constrain access in many developing countries. In addition, the advertising and promotion of cigarettes tends to be less restricted than that for NRTs in many countries.

Regulation of the consumer

Prescription requirements for NRT products are a significant effective restriction on consumers. In 7 out of 24 countries in Europe for which data are available, prescriptions are required for nicotine patches, and are required everywhere for nasal spray (IMS Global Services 1998). An extreme form of consumer regulation is in Japan, where NRT products may be sold only to smokers who suffer a tobacco-related disease. Currently, regulations prohibiting the sales of tobacco products to minors exist in only 43 of 134 countries surveyed by the WHO in 1995 (WHO 1997). But these regulations are usually ineffective or not enforced, as discussed by Woollery *et al.* in Chapter 11. Youth sales of NRTs are limited because, even where they are sold OTC, purchase by under-age consumers is prohibited.

12.3.5 Affordability: the cost of using NRT to quit

Most spending on NRT products is out-of-pocket. Insurance programs rarely cover the costs of NRT products, even in high-income countries. So household income and NRT prices are important determinants of access to NRT.

NRT expenditures vary widely across countries by income group. Based on data from IMS Global Services (1998) we calculate that in the United States, consumers spent \$10.88 per smoker on NRT products in 1996. In other high-income countries, consumers spent on average \$1.63 per smoker. Consumers in upper-middle-income countries spent \$0.03 per smoker. NRT prices in the United States tend to be considerably higher than elsewhere, except in Japan,² where NRT products cost nearly twice as much as in the United States. Figure 12.1 compares the weighted average prices of a standard NRT unit (one patch or one piece of gum) in 14 countries, using a

² For more information about Japan's unique pharmaceutical policy, see: Thomas III 1994.

NRT Products Per Standard Unit in Selected Countries, Relative to the United States, 1996

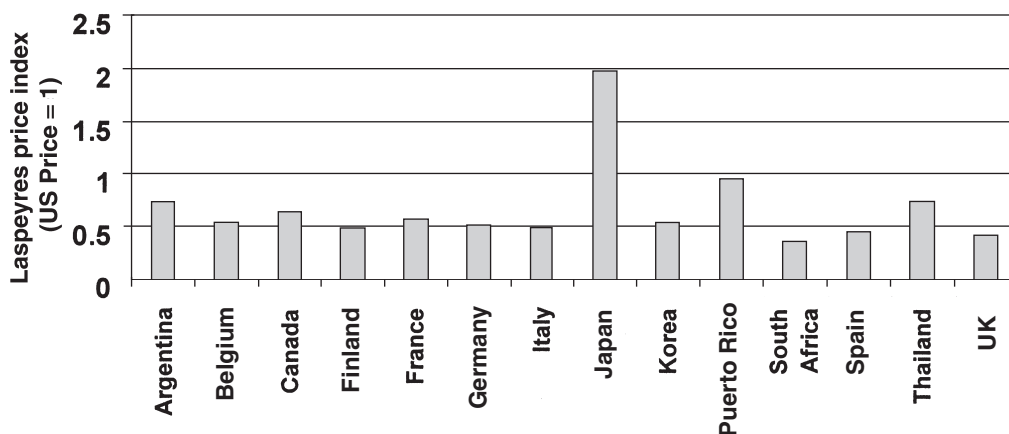


Fig. 12.1 Relative price of NRT products per standard unit in selected countries, 1996 (United States price = 1). Source: authors' calculations from World Bank data and IMS 1998.

Note: Laspeyres price index uses US NRT consumption as weights to estimate this index.

Laspeyres index, with the US price set to 1. NRT prices in several developing countries were between 25% and 35% lower than in the United States.

Whereas cigarette purchase is a long-term expense, the cost of NRTs is borne, at least in theory, over a limited period of a few months as smokers try to quit. We compared average annual spending on cigarettes per smoker (using average annual consumption and average price per pack) with the cost of a 3-month supply of NRT in 30 countries for which data were available. We assumed that 3 months' consumption would be the maximum usage of NRT products, given the usual recommendation that patches be used for up to 10 weeks. We assumed that consumers use one patch or 10 pieces of gum a day (well within the recommendation that no more than 20 pieces of gum be used per day). The costs are estimated for minimum and maximum prices of gums and patches.

For most industrialized countries, a 3-month supply of NRT products costs about half as much as a 1-year supply of cigarettes (Table 12.4). In developing countries, where cigarette prices are much lower, the cost of NRT for 3 months was equivalent to between one year's worth and four years' worth of cigarettes. In Argentina, it was 1.6 years, in Brazil 3.6–3.8 years, and in Indonesia, 7 years. However, these comparative figures probably do not capture very well the decision that the consumer makes. Even if consumers consider cigarettes and NRTs as substitutes to choose between at some point, their decision horizon may be relatively short, comparing the price of a pack or carton of cigarettes with a package or 1-week supply of NRTs. NRT gum is

Table 12.4 Costs of NRTs and cigarettes in selected countries, 1996

Countries	Annual cost of cigarettes in US\$	Cost of 3 months of NRT		Number of years of cigarette costs that are equivalent to 3 months of NRT	
		Patches	Gum	Patches	Gum
Argentina	191	316	358	1.7	1.9
Australia	1200	200–356	168	0.2–0.3	0.1
Austria	451	341–351	242	0.8	0.5
Belgium	881	367–385	186	0.4	0.2
Brazil	135	492–517		3.6–3.9	
Canada	613	328–377	248–518	0.5–0.6	0.4–0.8
Czech Rep	52	199	176	3.8	3.4
Finland	652	155–169	144–162	0.2–0.3	0.2
France	447	327–330	330	0.7	0.7
Germany	664	282–316	345	0.4–0.5	0.5
Greece	463	65–231	127–144	0.1–0.5	0.3
HongKong	211	352	270	1.7	1.3
Hungary	128		151		1.2
Indonesia	38		273	7.1	
Ireland	339	260–264	253	1.5–1.6	1.5
Italy	339	256–275	193–214	0.8	0.7
Japan	502		976–1010		1.9–2.0
Malaysia	127	271	287	2.1	2.3
Mexico	61	179–257		3.0–4.2	
Netherlands	474	271–288	228–287	0.6	0.5–0.6
New Zeal.	686	182–192	229	0.3	0.3
Norway	358	266–271	218	0.7–0.8	0.6
Poland	84	195		2.3	
Portugal	301	247–348	272	0.8–1.2	0.9
Singapore	475	240		0.5	
S. Africa	151	215–217	193	1.4	1.3
Spain	233	263–359	140–193	1.1–1.5	0.6–0.8
Thailand	64	412	222		3.4
UK	770	213–235	163–175	0.3	0.2
US	479	400–472	441–745	0.8–1.0	0.9–1.6

Source: authors' calculations from IMS Global Services (1998) Medical Information Database.

usually sold in packs of 32–120 pieces, and patches in packs of 7–32. Their price ranges across countries from \$7 in the Netherlands to \$65 in Puerto Rico per pack of gums, and from \$11 in Venezuela to \$65 in France per pack of patches. In contrast, average cigarette pack prices range from a few cents to \$1.50 in low-income and middle-income countries, and, even where prices are highest in some Scandinavian countries, rarely

exceed about \$7 (see Chapter 10). In many low-income countries, single cigarettes are sold on the street.

12.4 Policy options for governments

Given the currently limited market for NRT products, what are the implications for possible government intervention? Three broad areas of intervention are possible. They are: providing better information; changing the regulatory environment; and the financing of NRT products.

12.4.1 Information

The quantity of NRTs demanded appears small in the low-income and middle-income countries compared with the high-income countries. This is probably because fewer smokers in the low-income and middle-income countries are trying to quit, and because of the high prices and limited availability of the products. Government efforts to inform consumers better about the risks of smoking and the benefits of cessation are warranted on purely public goods criteria (see Chapter 8 for more detailed discussion on consumer information). There may be little justification for governments to intervene to publicize the benefits of NRT *per se*. However, many economists consider that there is a justification for publicizing the benefits of quitting (see Chapter 7).

12.4.2 Changes in regulations

As we have shown, the regulation of pharmaceutical nicotine products is considerably more extensive than the regulation of cigarettes. This gives cigarettes market advantages. Cigarettes are liberally marketed and harmful, while NRTs are more regulated but can reduce health damage from smoking. The tobacco industry has long-standing knowledge of the role of nicotine in initiating and sustaining cigarette consumption (Hurt and Robertson 1998). Given these imbalances, some analysts have argued that a consistent and integrated regulatory environment should in future be applied to all nicotine products. There is debate about whether NRT products should be deregulated so that they can compete more effectively with cigarettes and other tobacco products, or whether, instead, cigarettes ought to be more regulated or restricted (Kessler *et al.* 1997). The debate, however, is largely academic. If existing pharmaceuticals safety standards were applied to tobacco products, they would likely have to be removed completely from the market, or strictly regulated, because they are so hazardous. But market and political realities make such strict regulation impossible. Deregulating nicotine may be easier to implement and is more justifiable in economic terms (Sweanor 1998).

The liberalization of NRT markets could have significant health benefits if it resulted in increased cessation rates. However, opening the nicotine market without additional controls on tobacco marketing could potentially have significant adverse impacts on health behavior. These include the following:

- (1) NRT products could become gateway products for tobacco use;
- (2) they might be viewed as a substitute for cigarettes;
- (3) they might reassure smokers that they can delay cessation, and suggest to children that their risk of long-term addiction is reduced;
- (4) they could encourage lapsed smokers to start again;
- (5) they might not be effective among non-addicted smokers and could, thus, be perceived as generally ineffective in supporting cessation; and
- (6) ineffective or harmful products might become available with resultant adverse consequences.

To help limit some of these negative potential consequences, effective policies for pricing, regulation and information dissemination, both on tobacco use and NRT products, would be essential accompaniments to any increased availability of alternative pharmaceutical products. In addition, it could be beneficial to liberalize the criteria for marketing these products. Below we discuss several changes to NRT regulation that could increase the use of these products.

12.4.3 Reducing barriers to entry

Within overall trade policies, trade and non-trade barriers to NRT products can be reduced. One specific effort involves international harmonization of national pharmaceutical registration procedures, so that countries adopt consistent standards. Such harmonization could help make NRT products and other pharmaceutical products more widely available in the global market. Efforts at pharmaceutical harmonization are already underway regionally and inter-regionally. The European Union is the first region to harmonize pharmaceutical registration as part of its efforts to create a single market that allows for free trade in pharmaceuticals (IFPMA 1997). Mercosul (Argentina, Brazil, Paraguay, and Uruguay) countries have also taken steps to harmonize their drug registration procedures.

The International Conference on Harmonization of Technical Requirements for the Registration of Pharmaceutical Products for Human Use (ICH) is another international effort to standardize drug registration procedures. The ICH is focused on drug-registration procedures in Japan, the United States, and member countries of the European Union, but it is likely that its procedures will be extended to other countries as well. The ICH is working towards the harmonization of drug registration procedures for new products that demonstrate safety, efficacy, and quality. The potential benefits include cost savings through the elimination of duplicated registration procedures, more rapid entry of new products, and greater certainty of quality and safety standards.

Equally important, the harmonization of drug regulations may lower costs for pharmaceutical companies and make market entry more attractive. This, in turn, may provide incentives for further product development. Harmonization may be particularly useful for many low-income and middle-income countries where the burden of smoking is highest, financial resources are limited, and institutional capacity may be weak.

12.4.4 Reducing regulation of the provider, seller, or the conditions of sale

As discussed above, the regulation of NRT sales is often strict. There is evidence that deregulation, such as making sales available OTC, increases the use of NRT products in high-income countries. In 1986, the US Food and Drug Administration gave OTC approval to the nicotine transdermal patch and gum. As a result, NRT use increased dramatically. In 1995, an estimated 2.5 million quit attempts were made using prescription NRT products. In 1997, there were about half a million quit attempts using prescription NRT, and on conservative estimates, 5.8 million quit attempts used OTC NRT. Shiffman *et al.* (1997) suggest that, in addition to those who would have quit on baseline levels, between 114 000 and 304 000 Americans successfully quit smoking in 1997, due to the greater availability of NRT OTC range. In California, sales of NRT, both under prescription and OTC, are statistically associated with reduced cigarette consumption (Hu *et al.* in press).

12.4.5 Financing NRT

A priori, there is little government justification for paying for or subsidizing NRT products, because they are largely private goods. However, as noted in Chapter 7, there may be an argument for governments to directly fund pharmaceutical quitting aids for the poor in order to reduce price constraints that limit access. In the United Kingdom, for example, the government has introduced limited free NRT treatment under its National Health Service, with the goal of targeting the poorest (United Kingdom Department of Health 1998). There are theoretical gains in efficiency and equity if cigarette taxes are used to finance NRT for the poorest smokers.

We have estimated the number of smokers for whom governments could subsidize cessation aids by using the revenues generated from a 10% tax increase. We used a price elasticity of -0.4 for developed countries and -0.8 for developing countries. Estimating the revenue effect of changes in excise rates is reasonably straightforward (see Chapter 10 and Chapter 17). Based on the costs of gums and patches per smoker estimated above, we found that the additional revenues could subsidize between 3% and 30% of smokers in developed countries (Table 12.5). In the developing countries for which estimates were possible, fewer than 2% of smokers could be subsidized because tax rates and cigarette prices are low and NRT product prices are relatively high. In addition, the difficulties of targeting NRT subsidies to the poorest are considerable, as they are with many health interventions (World Bank 1993).

12.4.6 The cost-effectiveness of NRT

To consider including NRT in a basic universal package of clinical services in low-income and middle-income countries available to poor *and* non-poor smokers (World Bank 1993), governments would need to consider the burden addressed by smoking,

Table 12.5 Proportion of smokers who could receive subsidized NRT with an excise tax increase of 10%, selected countries, 1999

	Percentage of smokers that could be subsidized
High-income countries	
Greece	32.0
Australia	25.0
Finland	18.5
New Zealand	17.3
United Kingdom	15.6
Germany	10.3
Singapore	9.8
Canada	9.4
Belgium	8.6
Norway	7.1
Austria	6.8
Ireland	6.7
France	6.5
Italy	6.1
Portugal	6.1
Netherlands	5.5
Spain	4.7
United States	3.1
Low- and middle-income countries	
Czech Republic	1.8
Argentina	1.7
Poland	1.5
South Africa	1.3
Malaysia	1.0
Mexico	0.9
Brazil	0.6
Thailand	0.4

These estimates are based on expected revenue increase from a 10% increase in cigarette excise tax (see Chapter 17 for details), and the average cost of NRT in these countries if used for 3 months.

Source: authors' calculations from World Bank data and IMS Global Services (1998) Medical Information Database.

which is considerable, and the cost-effectiveness of the intervention. There have been few cost-effectiveness studies of NRT in low-income and middle-income countries. Ranson *et al.* (Chapter 18) have made some estimates. These suggest that, assuming public finance and an effectiveness of 2.5%, NRTs could cost about \$276 per disability-adjusted life-year (DALY) in low-income and middle-income countries. This would be regarded as broadly cost-effective; the World Bank suggests that health inter-

ventions that can be delivered for less than the average per capita GDP of a country are cost-effective (low-income countries are defined as those with a per capita GDP of \$765 or less). In high-income countries, the cost-effectiveness of smoking cessation has been established (USDHHS 1990; Curry *et al.* 1995; Fischle and Franks 1996; Cromwell *et al.* 1997; Wasley *et al.* 1997). Although the cost-effectiveness of short, provider-assisted smoking cessation has also been established (Cummins *et al.* 1989), such interventions still depend on physician action and patient access to medical care. Cromwell *et al.* (1997) determined that implementing the AHCPR guidelines on smoking cessation across the United States, which include costs of physician advice, counseling, NRT, and other therapies costs, would cost approximately \$3 500 per additional quality-adjusted life-year (QALY) saved. Greater cost-effectiveness was found in the interventions using NRT. The authors compared this cost to the cost of mammography screening (which exceeds \$61 000 per QALY) and hypertension screening (which exceeds \$23 000 per QALY).³

Cost-effectiveness studies of cessation therapies are complicated because there are many different pharmaceutical cessation treatments sold in different package configurations, through different distribution networks, with different concomitant counseling or treatment, and in countries with varied regulatory regimes for such products. In addition, those seeking to quit smoking do not necessarily use cessation products appropriately.

Analyses of the cost-effectiveness of NRTs often fail to take into account two key factors. First is the total cost of cigarette consumption. This is important since consumers are substituting one good (cessation products) for another, inferior, good (Warner *et al.* 1997, 1998). If the savings on tobacco products (and the other costs associated with the use of these products) are not taken into account, opportunity costs are missed out of the assessment. Second, some of the costs associated with cessation therapies can be attributed to government-induced regulation, such as restrictions on sales outlets and promotional activities. It should be noted, however, that if health insurers do not cover OTC products, and NRT products are not available by prescription, patients face higher out-of-pocket costs (Smeeth and Fowler 1998).

12.4.7 Mandating insurance coverage of NRT

Aside from direct finance, governments may also be able to mandate the coverage of key items through public or private insurance schemes (Musgrove 1999). Most insurers, with the exception of a few companies in the United States, do not reimburse for NRT products. Only 6 of the 51 state-funded insurance programs for the poor in the United States cover smoking-cessation programs (CDC 1999b). One report found that general smoking-cessation services were available in two-thirds of HMO health-financing plans sampled. The nicotine transdermal patch was covered by 64% of the plans, and nicotine gum by 44%. These programs usually required members to enroll

³ The cost per QALY reflects attributable doctor and patient time at US wage rates, and is not representative of such costs in lower wage economies.

in or complete a smoking cessation class as a condition of coverage, or to make out-of-pocket payments for NRT (Pinney Associates 1995).

In Australia in 1995, the federal government rejected a recommendation made by the Pharmaceutical Benefits Advisory Committee that NRT qualify for a (capped) subsidy under the Pharmaceutical Benefits Scheme (PBS). As the health minister explained at the time, the cost would have been prohibitively expensive, both in terms of the PBS and the impact of increased prescription costs under the Medicare program (Scollo 1995). By comparison, a recent study in the United States of the use and costs of cessation services among fully insured persons estimated the average cost at \$328 per user. This one-time cost compares favorably with the annual cost of treating heart disease (\$6 941) or hypertension (\$5 921), which persist over the life of the patient (Curry *et al.* 1998).

In sum, the arguments in favor of direct public finance for NRT, or the mandating of insurance coverage for it, are less clear than the case for deregulating access to these therapies and their use. Further cost-effectiveness studies are required to inform national policy.

12.5 Conclusions

Tobacco products are a major cause of ill health and premature death. Smoking cessation is a critical element of tobacco control, but information about the benefits of smoking cessation aids, their effectiveness, and their cost-effectiveness, is generally deficient in low-income and middle-income countries. Although nicotine is the addictive agent in tobacco products, it is the delivery vehicle rather than the nicotine in these products that causes the harm. Thus, cessation and reduction of tobacco use, using approved pharmacotherapy for continuing smokers, is a reasonable objective for public health. Yet these products are often not available at all in developing countries, are not competitively priced, or face regulatory limitations on availability and indications for use. The market for nicotine is largely deregulated for cigarettes, but regulated for NRTs.

NRT and other pharmacological treatments for nicotine addiction are comparatively safe if used as directed, and they are unlikely to cause adverse behavioral, cardiovascular, or other health effects. Although additional research is necessary, the benefits of long-term NRT use among smokers who are unable to quit should be considered. In addition, more pharmacological products that assist cessation should be developed.

Governments may be able to improve the success of tobacco control efforts by helping to increase the availability and affordability of NRT and other devices. This could be done by deregulating the conditions for the sales of these products, and through regional and global harmonization of registration and regulation. However, the prospects for government financing of NRTs, even for the poor, appears limited. This is due to the relatively high cost of the products, the fact that they are a private good, and difficulties in targeting NRT subsidies to the poor.

NRTs are not solutions in themselves to the public health problem of cigarette use. Rather, their use must be considered as part of comprehensive prevention and cessation programs.

References

- American Psychiatric Association (APA) (1996). Practice guidelines for the treatment of patients with nicotine dependence. *Am. J. Psychiatr.*, **153**(10 Supplement), 1–31.
- Anthonisen, N. R., Connett, J. E., Kiley, J. P., Altose, M. D., Bailey, W. C., Buist, A.S. *et al.* (1994). Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1. The Lung Health Study. *JAMA*, **272**(19), 1497–505.
- Bal, D. G., Kizer, K. W., Felten, P. G., Mozar, H. N., and Niemeyer, D. (1990). Reducing tobacco consumption in California. Development of a statewide anti-tobacco use campaign. *JAMA*, **264**(12), 1570–4.
- Benowitz, N. L. 1998. *Nicotine Safety and Toxicity*. New York: Oxford University Press.
- COMMIT Research Group (1995). Community intervention trial for smoking cessation (COMMIT): I. Cohort results from a four-year community intervention. *Am. J. Public Health*, **85**, 183–92.
- Cromwell, J., Bartosch, W. J., Fiore, M. C., Hasselblad, V., and Baker, T. (1997). Cost-effectiveness of the clinical practice recommendations in the AHCPR guideline for smoking cessation. *JAMA*, **278**, 1759–66.
- Cummins, S. R., Rubin, S. M., and Oster, G. (1989). The cost-effectiveness of counseling smokers to quit. *JAMA*, **261**, 75–9.
- Curry, S. J., McBride, C. M., Grothaus, L. C., Louie, D., and Wagner, E. H. (1995). A randomization trial of self-help materials, personalized feedback, and telephone counseling with non-volunteer smokers. *J. Consult. Clin. Psychol.*, **63**, 1005–14.
- Curry, S. J., Grothaus, L. C., McAfee, T., and Pabiniak, C. (1998). Use and cost effectiveness of smoking-cessation services under four insurance plans in a health maintenance organization. *New Engl. J. Med.*, **339**, 673–9.
- Doll, R., Peto, R., Wheatley, K. *et al.* (1994). Mortality in relation to smoking: 40 years' observations on male British doctors. *BMJ*, **309**, 901–11.
- Fagerstrom, K. O., Tejding, R., Westin, A., and Lunell, E. (1997). Aiding reduction of smoking with nicotine replacement medications: hope for the recalcitrant smoker. *Tobacco Control*, **6**, 311–6.
- Fiore, M. C., Bailey, W. C., Cohen, S. J. *et al.* (1996). *Smoking Cessation*. Clin Pract. Guideline No. 18. Rockville, MD: AHCPR Publ. No. 96–0692 and www.ahcpr.gov/clinic/smoview.htm
- Fischle, K. and Franks, P. (1996). Cost-effectiveness of the transdermal nicotine patch as an adjunct to physicians' smoking cessation counseling. *JAMA*, **275**, 1247–51.
- Foulds, J. (1996). Strategies for smoking cessation. *British Med. Bull.*, **52**, 157–73.
- Fowler, G. (1998). Nicotine replacement therapy for a healthier nation. *BMJ*, **317**, 1266–7.
- Gallup Organization (1998). New Gallup survey reveals smokers' increased desire to kick the habit. *Press Release*. Princeton, NJ: Gallup Organization, October 20.
- Gupta, P. C., Mehta, F. S., Pindborg, J. J., Aghi, M. B., Bhonsle, R. B., Daftary, D. K. *et al.* (1986). Intervention study for primary prevention of oral cancer among 36 000 Indian tobacco users. *Lancet*, **1**(8492), 1235–9.
- Hurt, R. D., Sachs, D. P., Glover, E. D., Offord, K. D., Johnston, J. A., Dale, L. C. *et al.* (1997). A comparison of sustained-release bupropion and placebo for smoking cessation. *New Engl. J. Med.*, **337**, 1195–202.
- Hurt, R. D. and Robertson, C. R. (1998). Prying open the door to the tobacco industry's secrets about nicotine. *JAMA*, **280**, 1173–81.
- Hu, T., Sung, H., Keeler, T., Marciniak, M., Keith, A., and Manning, R. (in press). *Cigarette Consumption and Sales of Nicotine Replacement Products*.
- IMS Global Services (1998). Medical Information Database (MIDAS)
- International Federation of Pharmaceutical Manufacturers Association (IFPMA) (1997). *Issues Handbook: Registration of Medicines and Harmonization*. Geneva: IFPMA.
- Jorenby, D. E., Leischow, S. J., Nides, M. A., Rennar, S. I., Johnston, J. A., Hughes, A. R. *et al.*

- (1999). A controlled trial of sustained-release bupropion, a nicotine patch, or both for smoking cessation. *New Engl. J. Med.*, **340**, 685–91.
- Kamat, V. R. and Nichter, M. (1998). Pharmacies, self-medication and pharmaceutical marketing in Bombay, India. *Soc. Sci. Med.*, **47**, 779–94.
- Kessler, D. A., Barnett, P. S., Witt, A. *et al.* (1997). Legal and scientific basis for FDA's assertion of Jurisdiction over cigarettes and smokeless tobacco. *JAMA*, **277**, 405–9.
- Miller, L. and Griffith, J. (1983). A comparison of bupropion, dextroamphetamine, and placebo in mixed-substance abusers. *Psychopharmacology*, **80**, 199–205.
- Mudde, A. N. and De Vries, H. (1999). The reach and effectiveness of a national mass media-led smoking cessation campaign in The Netherlands. *Am. J. Public Health*, **89**(3), 346–50.
- Musgrove, P. (1999). Public spending on health care: how are different criteria related? *Health Policy*, **47**(3), 207–23.
- Novotny, T. E. (1988). Cessation of smoking and the social milieu. (Editorial.) *Mayo Clin. Proc.*, **63** 729–31.
- Novotny, T. E., Romano, R. A., Davis, R. M., and Mills, S. L. (1992). The public health practice of tobacco control: lessons learned and directions for the states in the 1990s. *Ann. Rev. Public Health*, **13**, 287–318.
- Orleans, C. T., Schoenbach, V. J., Wagner, E. H. *et al.* (1991). Self-help quit smoking interventions: effects of self-help materials, social support instructions, and telephone counseling. *J. Consult. Clin. Psychol.* **59**, 439–48.
- Peto, R., Chen, Z. M., and Boreham, J. (1999). Tobacco: the growing epidemic. *Nature Medicine*, **5**(1), 15–17.
- Pinney Associates (1995). *Smoking Cessation and Managed Care*. Bethesda, MD: Pinney Associates.
- Porter Novelli Associates (1997). *Perceptions About the Effects of Tar and Nicotine*. April 2, 1997. Survey sponsored by SmithKline Beecham.
- Prochaska, J. O. and DiClemente, C. C. (1983). Stages and processes of self-change of smoking: toward an integrative model of change. *J. Consult. Clin. Psychol.*, **51**(3), 390–5.
- Raw, M., McNeill, A., and West, R. (1999). Smoking cessation: evidence-based recommendations for the healthcare system. *BMJ*, **318**(7177), 182–85.
- Room, R. (1997). Control systems for psychoactive substances. 1997. Workshop Presentation: *Alternative Nicotine Delivery Systems—Harm Reduction and Public Health*. Toronto, March 21–23, 1997.
- Schneider, N., Olmstead, R., Nilsson, F. *et al.* (1996). Efficacy of a nicotine inhaler in smoking cessation: a double-blind, placebo controlled trail. *Addiction*, **91**, 1293–1306.
- Scollo, M. (1995). *Statement of Rejection of PBAC Recommendation on Nicotine Patches*. Commonwealth Government. Canberra: Memo.
- Scrip Magazine*, 1999, 75, 29–32. Anon. 'World Market Data: Slow but steady for world pharma sales.'
- Shiffman, S., Gitchell, J., Pinney, J. M., Burton, S. L., Kemper, K. E., and Lara, E. A. (1997). The public health benefit of over-the-counter nicotine medications. *Tobacco Control*, **6**, 306–10.
- Shiffman, S., Mason, K. M., and Henningfield, J. E. (1998). Tobacco dependence treatments: Review and prospectus. *Ann. Rev. Public Health*, **19**, 335–58.
- Silagy, C. (1994). Nicotine replacement therapies in smoking cessation. *Biomedicine and Pharmacotherapy*, **48**, 407.
- Silagy, C., Mant, D., Fowler, G., and Lodge, M. (1994). Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. *Lancet*, **343**, 139–142.
- Sinclair, H. K., Bond, C. M., Lennox, A. S. *et al.* (1998). Training pharmacists and pharmacy assistants in the stage-of change model of smoking cessation: a randomised controlled trial in Scotland. *Tobacco Control*, **7**, 253–61.
- Smeeth, L. and Fowler, G. (1998). Nicotine replacement therapy for a healthier nation—nicotine replacement is cost effective and should be prescribed on the NHS. *BMJ*, **317**, 1266–7.

- Sweanor, D. T. (1998). The regulation of tobacco and nicotine: the creation, and potential for resolution, of a public health disaster. *Drugs: Education, Prevention, and Policy*, **5**.
- Thomas III, L. G. (1994). Pricing, regulation, and competitiveness: lessons for the US from the Japanese pharmaceutical industry. *Pharmacoeconomics*, **6**, Suppl. 1, 67–70.
- United Kingdom Department of Health (1998). *Smoking Kills: a white paper on tobacco*. London: the Stationary Office. (<http://www.official-documents.co.uk/document/cm41/4177/4177.htm>)
- US Centers for Disease Control and Prevention (1999a). Cigarette smoking among adults—United States, 1997. *Morb. Mortal Wkly Rep.*, Nov. 5, **48**(43), 993–6.
- US Centers for Disease Control and Prevention (1999b). *Best Practices for Comprehensive Tobacco Control Programs*. Atlanta GA: US 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.
- US Dept of Health and Human Services (1988). *The Health Consequences of Smoking—Nicotine Addiction*. A Report of the Surgeon General. Rockville, Maryland: US Dept of Health and Human Services, Public Health Service, Centers for Disease Control, Center for Health Promotion and Disease Prevention, Office on Smoking and Health; DHHS publication no. (CDC)88–8406.
- US Dept of Health and Human Services (1990). *The Health Benefits of Smoking Cessation*. A Report of the Surgeon General. Rockville, Maryland: Office on Smoking and Health; DHHS publication no. (CDC) 90–8416.
- Vartiainen, E., Korhonen, H. G., Koskela, K., and Puska, P. (1998). Twenty year smoking trends in a community-based cardiovascular diseases prevention programme—results from the North Karelia Project. *Eur. J. Public Health*, **8**, 154–9.
- Warner, K. E., Slade, J., and Sweanor, D. T. (1997). The emerging market for long-term nicotine maintenance. *JAMA*, **278**, 1087–92.
- Warner, K. E., Peck, C. C., Woosley, R. L. *et al.* (1998). Treatment of tobacco dependence: innovative regulatory approaches to reduce death and disease. *Food and Drug Law J.*, **58**, 1–8.
- Wasley, M. A., McNagny, S. E., Phillips, V. L., and Ahluwalia, J. S. (1997). The cost-effectiveness of the nicotine transdermal patch for smoking cessation. *Prev. Med.*, **26**(2), 264–70.
- World Bank (1993). *World Development Report 1993: Investing in Health*. Washington, DC: World Bank Publications.
- World Health Organization (1994). *International Statistical Classification of Diseases and Related Health Problems, Volume 3*, Geneva: World Health Organization.
- World Health Organization (1997). *Tobacco or Health: A Global Status Report*. Geneva: World Health Organization.
- World Health Organization (1999). *World Health Report: Making a Difference*. Geneva: World Health Organization.

