Smoking cessation: a European perspective

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Burden of disease

The medical community has only recently begun to accept tobacco dependence as a disease rather than a vice. The rate of clinical acceptance is slow, given that the World Health Organization (WHO) recognized tobacco dependence as a condition in its own right in 1992 in its International Classification of Diseases (ICD-10) (WHO 1992).

Tobacco dependence is a chronic, relapsing disease. In 2003, the WHO estimated that tobacco use would be responsible for approximately 5 million deaths worldwide. At the time of estimation, tobacco use was already responsible for 1 in 10 adult deaths, a figure that is expected to rise to one in six by 2030 (WHO 2003). If current trends persist, more than half a billion people will die through tobacco dependence this century (WHO 2003). In 2000 alone, tobacco use was responsible for 655,000 deaths among the European Union's (EU) 25 member states. The main causes of death included: cancers (285,000); cardiovascular disease (183,000); respiratory disease (113,000) and various other conditions (74,000) (Peto et al 2006).

Despite high tobacco-related mortality rates, a significant proportion of smokers fail to recognize or accept the dangers of their tobacco dependence. Moreover, many remain unaware that intensive treatment is available that could significantly improve their chances of quitting successfully. In Europe, the United Kingdom (UK) leads the way in smoking cessation provision through its National Health Service (NHS). Unfortunately, the benefits of smoking cessation as an effective healthcare intervention are not equally recognized throughout all EU member states. While some countries offer support as part of their normal healthcare systems, it is sadly not the case across the continent.

Changing attitudes

In recent years, however, there has been an awakening of consciousness in both the medical community and the public as to the irrefutable health implications of tobacco dependence and the benefits afforded by smoking cessation. Improved education and the introduction of legislation and national smoking bans have undoubtedly played a role in this heightened awareness. As a result, there is a growing realization among physicians of the role of effective smoking prevention therapies. Yet, many smokers still fail to make use of the available pharmacological and behavioral/psychosocial interventions.

Pharmacological interventions

In terms of pharmacological support, nicotine replacement therapy (NRT) has been available since the 1980s and bupropion since 2000. Either approach to cessation doubles the chance of achieving abstinence when compared with unsupported quit attempts (Stead et al 2008). Following its European license in 2006, varenicline (Champix®, Pfizer) joined the armamentarium of smoking cessation pharmacotherapy. Varenicline

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is the first drug developed specifically for the treatment of tobacco dependence that contains no nicotine, and it triples smokers' chances of quitting compared with unsupported quit attempts (Cahill et al 2007). Other approaches to assisted smoking cessation (such as the possibility of a nicotine vaccine) are currently under development.

Varenicline

It is widely accepted and understood that nicotine in cigarettes causes functional and structural changes within the brain. The highly addictive nature of nicotine is a result of the speed with which it reaches its peak levels in the bloodstream after inhalation – a speed that no smoking cessation products are able to replicate. Consequently, research and development in smoking cessation moved away from use of a full agonist and towards the use of a partial agonist, which acts as both an agonist, mimicking the effects of nicotine (albeit reaching peak levels in the bloodstream more slowly), and simultaneously as an antagonist, preventing nicotine from binding to its receptors in the brain.

Varenicline is the result of this change in approach to development of smoking cessation agents. It is a molecule based on cytisine and is a 40%–60% partial nicotine agonist. With a half-life of 24 hours, it does not interfere with cytochrome P450 and is barely metabolized within the human body (90% is excreted in urine in an unchanged form).

The agent has a dual mode of action. The first is the suppression of nicotine withdrawal symptoms, achieved by its binding to $\alpha 4\beta 2$ nicotinic acetylcholine receptors in the ventral segmental area of the brain: the receptor typical of a strongly addicted smoker. Once varenicline has bound to the receptor, an ion channel opens that allows ions to enter the neuron in the same way as occurs after nicotine binding. The resultant electrical signal causes the release of dopamine in the nucleus accumbens, which suppresses withdrawal symptoms ("agonistic activity"). In its second mode of action, through binding to the appropriate receptors in the brain, varenicline inhibits the ability of nicotine binding of the already occupied receptors ("antagonistic activity"). From my own clinical experience, the result of varenicline's dual effect is that patients do not complain of withdrawal symptoms such as anxiety, depression and poor concentration, and they report the absence of their normal desire to smoke. Furthermore, due to varenicline's antagonistic activity, those who continue to smoke report a lack of the standard reward attained from cigarette smoking.

Various trials of varenicline in patients have found its short- and long-term efficacy to exceed that of both placebo and sustained-release bupropion (Zyban®) (Gonzales et al 2006; Jorenby et al 2006; Králíková 2006; Tonstad et al 2006). In addition to varenicline's positive efficacy data, it has a favorable adverse events profile. Nausea is the most common side effect reported in patients receiving varenicline, up to 30% in clinical trials but about 20% in practice, from my own clinical experience. Overall, however, it is deemed to have a favorable safety profile (Gonzales et al 2006; Jorenby et al 2006; Králíková 2006; Tonstad et al 2006). The reported nausea tends to occur at the beginning of treatment and usually improves (and often disappears) with time. With a view to minimizing chances of initial nausea, the dosage should be slowly titrated up to the recommended 1 mg twice-daily dose.

Approved by the Food and Drug Administration (FDA) in the USA and by the European Medicines Agency (EMEA) in Europe in 2006, varenicline has been available in almost all European countries since the beginning of 2007 (or is planned for immediate release). The agent is licensed for smoking cessation in adults and is indicated for use for 12 weeks (Pfizer Limited 2007).

The trial data certainly suggest that at this time, varenicline appears to be the most effective smoking cessation treatment available, increasing quit success rates three-fold when compared with placebo (Gonzales et al 2006; Jorenby et al 2006). Furthermore, trial data demonstrated a 44% quit rate at 1 year in patients who were prescribed an additional 12-week course of varenicline after managing to quit in the first 12-week treatment period with the agent. Compared with a 37% abstinence rate at one year in those patients who had successfully quit in the first 12 weeks, but who received placebo for the additional 12-week period, these data suggest that varenicline may have greater benefit if taken for longer than the licensed 12-week period (Tonstad et al 2006). These findings have been supported in practice and with data from a cohort of psychiatric patients (Stapleton et al 2007). Clinical opinion follows that there may be benefit in recommending a treatment duration longer than 12 weeks, since tobacco dependence is a chronic, often relapsing disorder and some nicotine withdrawal symptoms may last for more than 3 months.

Clinical experience from across Europe

This publication aims to identify key elements of successful smoking cessation programs by bridging experiences of intervention adoption and subsequent reimbursement, discussing aspects of successful cessation programs and highlighting the territory-specific nature of some of the issues reported.

The body of evidence on varenicline will continue to grow over time, but the hope is that this collection of experiences from across the EU may offer insight to optimize the use of varenicline (and other smoking cessation agents), and help reduce the current and future health and social burdens associated with tobacco dependence.

What follows is a collection of experiences and views on smoking cessation from around Europe, supplied by national smoking cessation experts: Prof. Gérard Dubois from France; Dr Tobias Raupauch from Germany, Dr Diego Vanuzzo from Italy; Dr Jorn Ossum Gronert from Norway; and Dr Piotr Jankowski from Poland.

The authors consider the burden associated with smoking in their respective European territories and the changing attitudes toward smoking seen throughout the Continent; they compare the current state of national legislation on smoking bans and reimbursement; and assess the opinion of the pharmacological smoking cessation aids available. As the medical community is relatively familiar with NRT and bupropion, where possible, the focus will be on clinical experience with varenicline as a new treatment option in Europe. The level to which the reviews discuss varenicline reflects the amount of time it has been available in their respective territories. Some report solid data on the efficacy of the new agent, while others are limited by duration of experience to provide only a sense of how effective the agent is, based on their own clinical experience rather than hard and fast study data.

The Italian perspective

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Introduction

According to the WHO's European Tobacco Control Report 2007, the tobacco epidemic rages on across Europe and smoking remains a major contributory factor to the gap in mortality and life expectancy between the most- and least-advantaged members of society (WHO 2007a). Many initiatives have been undertaken to curb this situation at both international and national levels. Italy, for example, has a comprehensive official plan to promote a tobacco-free life (Italian Ministry of Health 2008), and has designated a section of the National Institute of Health to focus on smoking, alcohol and drug-related matter. The Observatory on Smoke, Alcohol and Drugs of Abuse (OSSFAD) serves as a highly qualified asset for health professionals and citizens (OSSFAD 2008).

This brief review aims to discuss: the prevalence and burden of smoking and smoking-related diseases in Italy; the Italian policy and attitudes towards smoking cessation and smoking bans; and current clinical experience with varenicline as a new smoking cessation treatment option. It will also consider the attitudes towards (and national policy on) adoption and reimbursement of smoking cessation products in Italy.

Smoking prevalence in Italy

The Italian National Institute of Statistics (ISTAT) carried out a health assessment of 60,000 households between December 2004 and March 2005. It revealed a 22.3% prevalence of current smokers among those aged 14 years or more, comprising 28.5% males and 16.6% females. Differences in prevalence between age-defined sub-groups are summarized in Figure 1 (ISTAT 2006, ISTAT 2007).

Daily cigarette smokers accounted for 89.7% of those who smoked; the average number of cigarettes smoked per day was 16.2 for men, and 12.4 for women. Among smokers, 45.5% of men and 25.9% of women were classified as heavy smokers (≥20 cigarettes a day) (ISTAT 2007). Approximately 51.9% of smokers had been smoking for ≥20 years The mean age at which they started smoking was 17.6 years for men, and slightly older (19.5 years) for women; however,

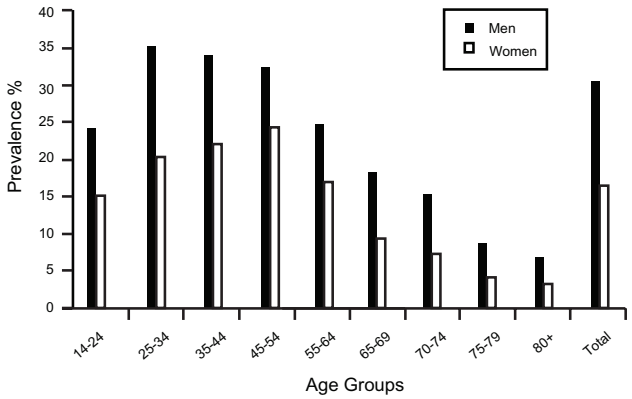

Figure 1 Current smoker prevalence in 2005 in Italy among those aged 14 years or more (redrawn from ISTAT 2007).

in the 14–29 years age group it was 17 years in both genders (ISTAT 2006).

When questioned about previous quit attempts, 21.9% of smokers, without significant gender differences, admitted to having tried to quit in the preceding 12 months. The prevalence of ex-smokers in the sample was 29.2% among men and 14.5% among women, with a mean "quit age" of 41.4 years for men and 38.0 years for women. The assessment also questioned quitters as to what level of assistance they received during their quit attempt. The majority of ex-smokers (93.4%) succeeded in giving up the habit on their own; only 2.7% quit with the assistance of their doctor and even fewer (0.8%) quit with the use of smoking cessation agents (ISTAT 2007).

A different survey, conducted in March and April 2007 by DOXA (the Italian branch of the Gallup International Association) on a representative sample of 3,057 Italians aged 15 years or over, showed a slight difference in the prevalence of smokers compared with that recorded in the ISTAT report: 27.9% for men and 19.3% for women. However, the main discrepancy with the ISTAT survey was the lower mean age at which both sexes started smoking: 15.7 years for men and 15.9 for women (OSSFAD DOXA 2007).

Smoking takes a major toll on health resources and the medical profession, yet, despite their detailed knowledge of the health risks associated with tobacco smoking, the prevalence of smoking among Italian physicians is particularly high (Smith and Leggat 2007): 25%–32% among male doctors and 20%–23% among female doctors (La Vecchia et al 2000; Pizzo et al 2003).

Burden of smoking and smoking-related diseases

The Italian Ministry of Health estimated that 81,855 deaths (15% of the national total) in the year 2000 were tobacco-related (see Table 1). More than a third of these deaths (34.4%) occurred in the 35–69 years age group (Italian Ministry of Health 2006).

The health implications of passive smoking are also significant. Table 2 summarizes some of the potential effects of passive smoking in Italy as assessed by Forastiere et al (2007).

Policy and attitude to smoking in Italy

According to the WHO's European Tobacco Control Report 2007, tobacco-control policies include: price and taxation; exposure to tobacco smoke; advertising, promotion and sponsorship; education, information and public awareness; smoking cessation; product control; consumer information; illicit trade; availability of tobacco to young people; and tobacco subsidies (WHO 2007a). For the purposes of this review, however, the discussions will focus on the Italian tobacco control policies aimed at passive smoking and smoking cessation.

Table 1 Tobacco-related deaths in Italy in the year 2000 (redrawn from Italian Ministry of Health 2006)

Causes of death	Men	Women	Total
Cancer	31,365	4,504	35,869
Cardiovascular disease	22,028	7,187	29,215
Respiratory disease	12,220	4,551	16,771
Total	65,613	16,242	81,855

Passive smoking legislation

With the objective of protecting citizens from exposure to passive tobacco smoke, a law banning smoking in enclosed public places came in to force in Italy on 10 January 2005 (Government of Italy 2003). The law forbids smoking in indoor areas, including hospitality venues and workplaces, unless there is a separate smoking room that includes mandatory features (President of Ministers' Council 2003).

A recent paper by Gorini et al presented a brief summary of the studies conducted in Italy in order to evaluate the impact of the ban (Gorini et al 2007). It found that public support of the ban increased after it was introduced. The surveys have concluded that the Italian public and owners of hospitality premises generally respect the ban. Assessment of atmospheric nicotine concentration in sample hostelries in Florence, and measurements of the concentration of particulate matter with diameter <2.5 μm in 50 hostelries

Table 2 Effects of passive smoking on the Italian population (redrawn from Forastiere et al 2007)

Population exposed	Outcome	Number of events
Newborn babies	Low birth weight (<2,500 g)	2,033
	Sudden Infant Death Syndromes	87
Children 0–2 years	Acute lower airways infections	76,954
	Bronchial asthma (prevalence)	27,048
Children and adolescents 6–14 years	Chronic respiratory symptoms (incidence)	48,183
	Otitis media (incidence)	64,130
Adult deaths	Lung cancer	545
	Ischemic heart disease	2,131

in Milan, Trieste and Rome, found a reduction of 70%–97% when comparing pre- and post-ban levels.

A fall in cigarette sales also followed the ban. Total cigarette sales in Italy decreased by 6.1% in 2005 compared with 2004, falling from 98.8 to 92.8 million kg. However, a slight increase (1.1%) in sales was seen in 2006 compared with 2005, which could be partly attributed to the provision of covered, outdoor smoking places by many restaurants and bars throughout the winter of 2005–2006.

Encouragingly, total sales of nicotine replacement products increased by 10.8% from January to September 2005 compared with 2004 sales (Galeone 2006). In addition, using hospital discharge records in the Northern Italian regions, Barone-Adesi et al estimated that there has been a significant decrease in the number of people under the age of 60 years who had been admitted for acute myocardial infarction (AMI) since the introduction of the ban. The hospital discharge records suggested that the sex- and age-adjusted admission rate for AMI among this patient group was 0.89 (95% CI 0.81–0.98) when comparing February-June 2005 with the same period in 2004. No difference in AMI admission rate was seen in those aged 60 years or above (Barone-Adesi et al 2006).

Smoking cessation promotion

In addition to the smoke exposure legislation discussed above, initiatives have also been taken in Italy to promote smoking cessation. These initiatives include: news releases and updated guidelines for health professionals by OSSFAD; provision of a quit phone line and an online inventory of existing smoking cessation clinics (also by OSSFAD) and the production and dissemination of educational materials for lay people.

In May 2007, there were 346 smoking cessation clinics operating within the Italian NHS (OSSFAD DOXA 2007). A prospective longitudinal multi-center study involving 41 of these services (across 16 different regions in Italy) and 1,226 patients (54.2% males, 45.4% females; mean patient age of 47 years) was conducted between April 2003 and June 2004. The cessation rate was found to range from 25% for patients receiving a single session of motivational counseling, to 65.3% for those receiving a combination of NRT and group therapy (Belleudi et al 2007). These data suggest a significant benefit in treatment outcomes though the use of pharmacological smoking aids.

Clinical experience with varenicline

In 2007, the Cochrane Collaboration reviewed the main studies on varenicline, which demonstrated its efficacy versus placebo and bupropion (Cahill et al 2007). The review concluded that varenicline increased the odds of successful long-term smoking cessation approximately three-fold compared with pharmacologically unassisted quit attempts and, in trials prior to the date of publication, more study participants had quit successfully with the aid of varenicline than with bupropion. Based on the study data available, the authors also concluded that the main adverse effect of varenicline is nausea, but that this mostly occurs at mild to moderate levels and tends to reduce with habituation. Yet, the authors also noted the need for further studies of varenicline against placebo, and against both bupropion and NRT, to establish the relative efficacy of the treatments.

Shortly after varenicline's introduction in Italy on 28 May 2007, start-up conferences were held in Rome (in June and July 2007) to inform medical opinion leaders and representatives of the existing network of smoking cessation clinics about the new smoking cessation product. As varenicline has not been in use in clinical practice for long at the time of writing, current experience is limited. However, some data are available about the number of smokers who have been prescribed varenicline since the week of its Italian launch (see Figure 2): in 5 months, more than 10,000 Italians have been given the varenicline starter pack (IMS 2007).

The manufacturers also carried out a survey to assess patients' attitudes and knowledge of varenicline and its correct usage. The study involved 150 expert physicians and consisted of online interviews conducted between 20 July and 17 August 2007. The findings were compared with those of benchmark interviews conducted earlier in the year (in March and April), prior to varenicline's launch. The physicians reported that two-thirds of the patients they treated correctly viewed the length of

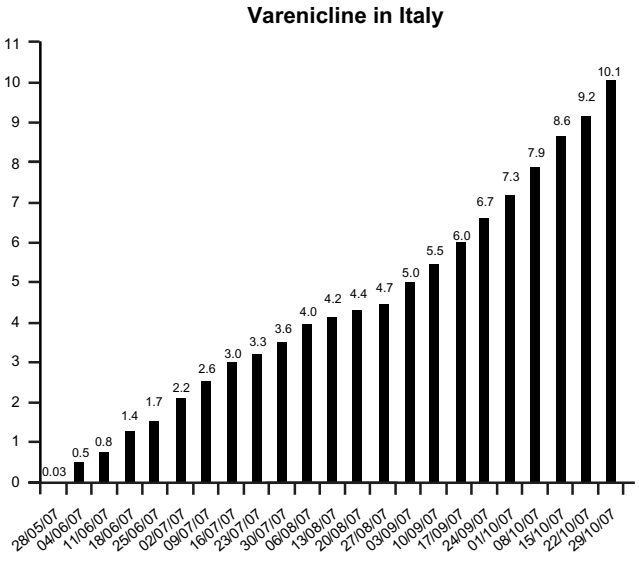

Figure 2 Number of smokers (cumulative 000) prescribed the varenicline starter pack in the five months following its May 2007 launch (IMS 2007).

varenicline therapy as 12 weeks. Of those remaining, the rest tended to believe the treatment period to be shorter. The interviewed physicians reported that 60% of treated patients completed the full length of therapy (LOT). Among those patients who did not complete the full LOT, the main reason for early discontinuation was a belief that they were already "cured".

Due to the limited time that varenicline has been available in Italy, direct comparison of its use against that of other smoking cessation agents is difficult, but it is certainly being used fairly widely for such a new agent. So far, 10,000 patients have been prescribed the starter pack compared with annual unit sales of approximately 500,000 per year for NRT and 9,000 for bupropion (Vasselli 2006).

Adoption and reimbursement

In Italy, NRT is available over the counter (OTC), while bupropion and varenicline are available by medical prescription only (WHO 2007a). As is the case in many other European countries, the Italian NHS does not reimburse smoking cessation products. Only Belgium, Cyprus, Denmark, France, Ireland, and the UK offer partial reimbursement of these products through their NHS. Furthermore, this partial reimbursement is generally restricted to assistance for those on lower incomes and/or those aged over 65 years.

There is strong Italian advocacy towards reimbursement of smoking cessation treatments by OSSFAD and by many professional and consumer associations. When the aforementioned DOXA survey directly asked those interviewed what they would like to ask of the Health Authorities in order to reduce smoking and promote smoking cessation, 83.6% of respondents requested free access to smoking cessation services, and 76% requested full reimbursement of smoking cessation drugs. At present, the Italian government's reticence to respond to such public opinion is based on its cost, in comparison to that of other priorities.

Conclusion

The national prevalence of current smokers in Italy in 2007 is 23.5%. Unfortunately, this compares with a professional prevalence of 25%–32% among Italian physicians, despite an estimated 81,855 tobacco-related deaths in the year 2000 (15% of the total annual national mortality). In addition, passive smoking is estimated to cause more than 177,000 cases of pediatric respiratory conditions and aural diseases, and more than 2,500 deaths annually in Italy.

Italy enforced legislation in January 2005 that bans smoking in enclosed public places, and findings of subsequent surveys suggest that the Italian public and owners of hospitality premises largely respect the ban. Changes in sales of tobacco and smoking cessation products suggest that the ban may be encouraging more Italians to give up smoking. Total annual sales of nicotine replacement products from January to September 2005 were up 11% from 2004. This is a promising sign, as is a 2004 study of some of Italy's smoking cessation services that reported a quit rate of 65.3% for those receiving a combination of NRT and group therapy, significantly higher than the 25% quit rate found in patients receiving a single session of motivational counseling alone. In addition, analysis of hospital discharge records in the Northern Italian regions indicates that there has been reduction in AMI admissions in patients less than 60 years of age since the introduction of the ban.

Successes in smoking cessation may be further aided by the introduction of varenicline, a new smoking cessation product that was launched in Italy on 28 May 2007. After only 5 months of use, it has been widely prescribed with more than 10,000 Italians having received the starter pack by the end of 2007. However, similar to bupropion, varenicline is available by medical prescription only, unlike OTC NRT products, and, despite public opinion, there remains no reimbursement of smoking cessation products or programs through Italy's National Health Service at this time.

The German perspective

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Prevalence and smoking burden

According to 2005 survey data, Germany has a smoking prevalence of 33% among men and 22% among women (Federal Statistics Office 2005). Smoking rates are slowly decreasing in the male population, but have continued to increase among women over the past 20 years (Lampert and Burger 2005). An additional cause for concern is the high smoking rate found in the group aged 12–17 years, 21% prevalence for boys and 19% for girls (BzgA 2005).

Smoking is estimated to be responsible for approximately 140,000 deaths in Germany every year (John and Hanke 2001). At least 30,000 of these deaths are attributed to cardiovascular disease caused as a direct result of smoking (Peto 2000), while another 2,150 annual deaths are attributed to cardiovascular disease resulting from passive exposure to smoke (Heidrich et al 2007).

The healthcare costs arising from smoking-related morbidity are substantial. Annual tobacco-related costs to the German healthcare system are estimated to exceed €35 billion (Criée and Nowak 2006). This contrasts to annual tax revenues from tobacco sales of approximately €15 billion (Bundestag 2007).

Policy and attitude to smoking

German public debate on banning smoking in public places was fuelled by a combination of increasing awareness of the burden of smoking-related disease, intensive media coverage of the dangers associated with passive smoking (Raupach et al 2006), and the effects of smoking bans (Sargent et al 2004; Barone-Adesi et al 2006; Bartecchi et al 2006). Public opinion was reflected in the enactment of the Act For Protection From The Dangers Of Passive Smoking on 1 September 2007. This law describes general measures to be taken to protect the population from the harmful effects of second-hand smoke, thus also setting the agenda for a comprehensive tobacco-control policy in Germany.

Unfortunately, responsibility for implementing the requirements of the Act resides with each of the 16 German states, all of which have subsequently devised specific rules and regulations. This has resulted in somewhat scattered legislation, with Bavaria adopting the strongest stance and Saarland providing its population with the weakest protection from second-hand smoke. Largely ignoring the encouraging and consistent findings from other countries (Glantz 2000; Scollo et al 2003; Luk et al 2006), where public smoking bans have not led to decreased revenues in bars and restaurants, some German trade unions are currently taking legal action against the public smoking ban. Thus, the situation remains unsettled.

Smoking cessation programs: clinical experience

A comprehensive review of cessation programs, their content and respective long-term continuous abstinence rates in Germany is beyond the scope of this article. Moreover, these data are difficult to obtain as only a few providers of cessation services have assessed their own results according to international standards (West et al 2005). The following section reports on success rates and predictors of long-term abstinence derived from an analysis of a validated 6-week group cessation program using pharmacological support. A concise description of course content and methodology can be found elsewhere (Raupach et al 2007a).

In brief, 369 subjects recruited from the general population and hospital staff took part in a cognitive-behavioral cessation program of 8-weekly sessions. Groups contained up to 14 patients and the participants each chose their own personal quit date at some point between the fourth and the fifth session. Various topics were covered during the group meetings, with the major issues including: mechanisms underlying nicotine addiction; enhancement of motivation to quit; relaxation training; coping skills; and development of strategies for relapse prevention.

The group had a self-reported quit rate of almost 80%, which was validated biochemically through exhaled carbon monoxide. Based on self-reported data, nearly a third (30%) of the groups' participants achieved continuous abstinence after 6 months. Further analysis showed that, during the first year after establishing the cessation service, there was a significant increase in long-term success rates (from 15% to 35%). The observed improvement in quit rates may have been positively influenced by the increased experience of the psychological support staff running the courses over time. This learning effect in the support staff should be accounted for when assessing success rates of newly set-up cessation services.

Pharmacological support

At the time of data collection, NRT and bupropion were the only pharmacological smoking cessation supports widely used in Germany. Varenicline was introduced to the German market only in March 2007, so national long-term abstinence in those taking this new drug cannot yet be reported. While NRT can be purchased without prescription (ie, over-the-counter [OTC]), bupropion has to be prescribed by a physician. Currently, smoking cessation agents are not eligible for reimbursement by German health insurers.

Although the use of nicotine replacement products was greatly encouraged during the sessions, only around half (n = 182) of all participants decided to take NRT (see Figure 3A). Of these, the majority (60%) used nicotine patches, 30% used nicotine gum or tablets and 10% used a combination of different NRT preparations. Across the 2-year period covered by our analysis, bupropion was used by an average of 10% of participants. However, reports of bupropion-related adverse effects influenced its level of usage, resulting in the percentage of participants using the

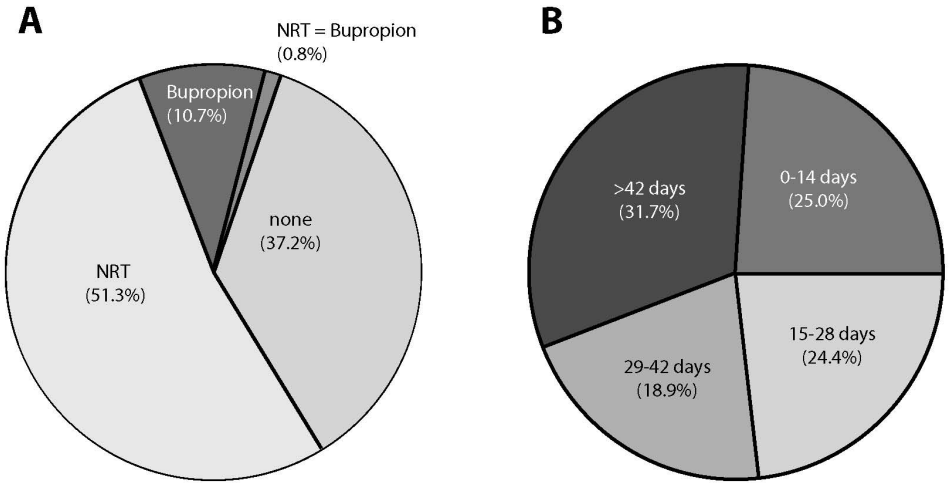

Figure 3 Use of pharmacological smoking cessation aids in 369 participants of a cognitive-behavioral group program (data derived from [Raupach et al 2007a]). (**3A**) distribution of substances used in the complete sample; (**3B**) therapy duration in the subgroup of participants (n = 182) taking NRT.

agent dropping from 20% in 2003 to 3% in 2005. In contrast, use of NRT over the same period increased from 40% in 2003 to 73% in 2005.

As was expected from the literature, NRT use compared to no medication nearly doubled success rates after 6 months (odds ratio [OR] = 1.83; 95% CI 1.10–3.03). However, 58.1% of NRT users discontinued their medication within the first 35 days of treatment (see Figure 3B), resulting in a median use of 30 days (range 1–270). The importance of this early discontinuation is 2-fold. Firstly, multivariate analysis of predictors of 6-month continuous abstinence showed that, apart from low scores for nicotine dependence (Heatherton et al 1991), a longer treatment course with NRT products was associated with significantly higher success rates: statistically, each additional week of NRT use yields a 10.4% increase in the probability of continuous abstinence for six months (Raupach et al 2007a). Secondly, the reasons for low NRT usage rates and early termination of NRT use in our sample need to be determined, as they combine to prevent optimum smoking cessation success with the available treatments. Studies are underway to assess new ways of motivating smokers to apply pharmacological support optimally.

The role of varenicline

The role of varenicline in the context of comprehensive cessation programs needs to be determined in randomized, controlled clinical trials. In Germany, it is available only by prescription and the cost of treatment is not reimbursable through health insurers. These two facts may pose a barrier to widespread use in the socially deprived, who are known to suffer the most from smoking-related mortality (Jha et al 2006). Demand for varenicline is relatively high and first results regarding treatment success are encouraging. However, as with NRT (Balfour et al 2000), patients tend to discontinue treatment before the recommended treatment period of 12 weeks has been completed. Although side effects of varenicline are usually mild to moderate in intensity and do not cause many patients to terminate its use, recent reports of more severe adverse events occurring during treatment warrant thorough evaluation (FDA 2007).

Smoking cessation and the German healthcare system

Education and training

Due to the lack of funding in the German healthcare setting for a specific cessation strategy with known effectiveness and efficacy, various cessation methods of differing qualities are currently available. A recent survey commissioned by the Federal Centre for Health Education and the German Cancer Research Centre revealed that among all providers of smoking cessation services, physicians are least aware of the most effective strategies to achieve long-term abstinence. Many offered acupuncture, even though this method was not found to be effective by the Cochrane Collaboration (White et al 2006). Intensive cessation programs have been implemented in some areas, but in regions where smoking rates are particularly high, such as Eastern Germany, the provision of services is not sufficient to meet the needs of the population. Data from the survey were first presented at

the fifth German Tobacco Control Conference in December 2007 (Bothe 2007), and publication of this comprehensive overview of validated cessation programs in Germany was expected in early 2008.

The results of a different survey carried out in German health institutions suggested that general practitioners (GPs) are the key players in promoting smoking cessation (Heilmann 2007). Yet, conflicting data from the Smoking and Nicotine Dependence Awareness and Screening Study revealed that the smoking status of German patients is not routinely assessed in primary care and that cessation advice is only offered to 40%–65% of all smoking patients (Hoch et al 2004). This may be because physicians involved in primary care do not feel adequately prepared to help smokers to quit. A questionnaire assessing physicians' activity in promoting smoking cessation surveyed 315 GPs from the Rhein-Neckar region of Germany and found that only 34.2% rated their training as adequate (Twardella and Brenner 2005). This notion is also supported by survey data from medical students (Brenner and Scharrer 1996; Raupach et al in press) and, more recently, by results from the Global Health Professionals Survey (Costa de Silva et al 2005).

For medical students in Germany, the situation is further aggravated by German medical textbooks, a considerable number of which contain misleading information on the role of nicotine in tobacco addiction and in the initiation and progression of cardiovascular disease (Raupach et al 2007b). This misconception may prevent young doctors from recommending pharmacological aids of proven effectiveness. Owing to the insufficient training of physicians on the topic of smoking, and in the practical skills needed to support those smokers willing to quit, the German Medical Association recently launched a curriculum addressing these issues.

Reimbursement

GPs' efforts to support smokers who are willing to quit are hampered by the lack of reimbursement of these activities. Patients seeking assistance with their quit attempt have to pay for all consultations and the recommended medication themselves. For participants of the cessation service mentioned above (Raupach et al 2007a), costs per life year gained were estimated at approximately €250 (Felten et al 2006). A recent randomized trial showed that provision of physician training and direct participant reimbursements for pharmacy costs significantly increases the odds of cessation (Twardella and Brenner 2007). In addition, the cost-effectiveness of NRT has been specifically shown for the German healthcare setting (Wasem et al 2007).

In view of the fact that smoking cessation is among the most cost-effective health interventions available (Tengs et al 1995), a policy change rendering cessation advice and pharmacological support amenable to reimbursement by health insurers has been called for (Raupach et al 2007c). At the same time, comprehensive provision of low-threshold cessation services to which smokers can be easily referred should be made a priority.

The French perspective

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Introduction

Tobacco is the only consumer product that, when used as intended rather than abused, kills half of its regular users (Doll et al 1994). It is the world's leading cause of avoidable deaths, making it a WHO priority. Although the first anti-tobacco association was established in France as early as 1868, the tobacco industry managed to prevent the product's health concerns from really penetrating the public consciousness throughout the first half of the 20th century. With proof of the dangers of tobacco smoking dating back to the 1950s, the WHO has established an international treaty (Framework Convention on Tobacco Control [FCTC]) that has been ratified by 152 countries worldwide, and which came into force on 27 February 2005 (WHO 2008). France was the first country to ratify the WHO treaty as an EU member (on 19 October 2004) and to ensure that the treaty's core principles were reflected in the country's own tobacco control policy.

History of smoking in France

Although Jean Nicot (whose name lives on as "nicotine") brought tobacco from Portugal to France in the 16th century,

it was the arrival of the cigarette that brought about real change. The cigarette made tobacco consumption easy by making it available for use without the need to prepare it personally. The design of the cigarette also allowed deeper inhalation, which increased addiction. Additionally, when production moved to an industrial scale at the end of the 19th century, cigarettes became more affordable for smokers.

As was the case in the rest of the world, smoking initially predominated in the male population in France, particularly among those of high socio-economic standing. Cigarette use spread rapidly during World War I and, over a period of 2 to 3 decades, it spread through the rest of French society, reaching a prevalence of 60% by the 1950s. Tobacco addiction among French women lagged behind that of men by some 20 years, after which it grew rapidly, but did not exceed a prevalence of 30%. Women, and later children, were heavily targeted by ruthless and relentless cigarette advertising (Dubois and Tramier 2001; Dubois 2003). After cigarette use became widespread, it took another 2 decades for the health consequences of tobacco smoking to emerge.

French non-governmental organizations

The French Association against Tobacco Abuse was the first French anti-tobacco non-governmental organization (NGO) and was established on 11 July 1868. Since that time, it has changed its name several times, but always retained the goal of tackling tobacco dependence: it has been called the Society Against Tobacco Abuse (1877), the League Against Tobacco Abuse (1939), Prevention of Smoking (National Committee for Clean Air) (1959) and, since 1968, it has been known as the National Committee Against Smoking.

Following the 1991 establishment of the Evin Law, which forbids smoking in collective workplaces and on public transport, and legislates tobacco advertising and packaging, the Alliance Against Tobacco (the Alliance) was founded, initially through the unification of six independent NGOs. Currently, the Alliance comprises 34 NGOs and strives to: develop and coordinate joint action; implement structured coordination of the efforts of the associations; maintain a regular flow of information; support and contribute to the implementation of the WHO FCTC, and participate in organization of major gatherings of the tobacco control community.

NGOs were not instrumental in the development of anti-tobacco policy until after the Evin Law, but their role increased significantly post-1991 through their efforts to help implement the advertising ban. The Alliance was also integral in the struggle for smoke-free public places. In October 2004, it published results of a poll revealing that two-thirds of French men and women were in favor of a comprehensive ban on smoking in cafes and night-clubs, while three-quarters supported a smoking ban in all restaurants and workplaces. The next year, the Alliance published a report on passive smoking, which helped lead to the smoking ban in all covered and enclosed public places as of 1 January 2008.

French tobacco legislation and regulation

In France, only licensed tobacconists are entitled to display and sell tobacco products. Some places, such as restaurants, are allowed to resell (without display) certain products to their costumers.

The Veil Law introduced the first regulations on tobacco in France in 1976, thanks to the efforts of Professor Maurice Tubiana. The legislation was well ahead of its time; it placed restrictions on advertising, established health warnings and banned smoking in hospitals. However, the tobacco industry shamelessly continued to exploit loopholes in the law.

The Evin Law came about later (10 January 1991) through the endeavors of and pressure from The Five Wise Men group (Dubois G, Got C, Gremy F, Hirsch A, Tubiana M). The law banned all direct and indirect tobacco advertising, removed tobacco from the consumer price index, established the principle of non-smoker protection and strengthened health warnings (eg, "Smoking can seriously harm your health"). A courtroom battle ensued between the tobacco industry and the National Committee Against Smoking, resulting in the legislation taking 10 years to come into force. It was only in 2006 that the French Supreme Court (Court de Cassation) finally ruled, "all forms of commercial advertising, no matter the media, that aim to directly or indirectly promote tobacco or a tobacco product are clearly prohibited".

New labeling and packaging legislation for tobacco products then came into force in December 2002. This aimed to eliminate misleading modifiers such as "light", "mild", and "ultra light". In March 2003, limits were set on the levels of tar, nicotine, and carbon monoxide in cigarettes, and health warnings were required to cover at least 30% of the packet on one side and 40% on the other side, with black letters on a white background. Later the same month, President Jacques Chirac presented a new Cancer Plan and declared "a war on tobacco" that would lead to a 40% increase in cigarette prices within a 2-year period.

In July 2003, new legislation banned the sale of cigarettes to minors (children below the age of 16 years), banned "kiddie packs" of less than 19 cigarettes (20 since the law of 26 July 2005) and increased the scope of the advertising ban to include cigarette papers. Despite all the positive steps that were seen earlier in the year, the Prime Minister signed an "armistice" with the tobacconists in November 2003 that blocked any new tax increases for 4 years. It was considered a "black day" for anti-smoking campaigners. There has since been a 6% growth in price, but as a result of industrial price increases, not taxation.

More recently, a new incarnation of the Evin Law, which bans smoking in all enclosed and covered public places, has been implemented. The workplace ban came into force on 1 February 2007, and the law prohibiting smoking in all other public places came into force 1 January 2008.

National prevalence and burden of smoking

The huge increase in cigarette prices that took place in 2003 (8.3% in January; 18% in October) and 2004 (8.5%) led to an unprecedented and unparalleled reduction in national tobacco sales. Tobacco sales dropped by 27%, cigarette sales dropped by 33% and the prevalence of daily smoking fell by 12%: overall, the number of smokers dropped by from 15.3 million to 13.5 million (Institut National de Prévention et d'Education pour la Santé [INPES] 2004) (see Figure 4).

In 2005, the prevalence of cigarette smoking (including occasional smoking) among men aged 12–75 years was 29.9%, having fallen from 33.1% in 2000 (INPES 2006). Over the same 5-year period, smoking prevalence among women aged 12–75 years fell from 29.9% to 26.6%; among boys aged 17 years, it fell from 41.9% to 33.6%; and among girls of the same age, from 40% to 32.3%. In 2000, the smoking prevalence among French adolescents was one of the highest in Europe, but with the overall prevalence among 17-year-olds having fallen to 33%, it is now comparable to the European average.

Despite a reduction in the smoking prevalence in France, the smoking-related death toll remains high. In 1999, an estimated 66 000 people died as a direct result of tobacco smoking (see Table 3) (Hill and Laplanche 2003), while passive smoking was responsible for a further 3000–5000 deaths (Dubois 2005; Dubois and Cornuz 2006).

However, it is hoped that these numbers will fall as a result of the smoking ban being implemented in public workplaces as of February 2007. Implementation of the workplace ban has so far proven to be very successful. Since its introduction, the number of highly smoke-polluted establishments has halved, and twice as many employees report that they are not exposed to smoke (80% in March 2007 compared with 42% in January 2007). There has also been a reduction in the number of employees reporting symptoms of irritation (both among smokers and non-smokers), but as yet, no decrease in myocardial infarction has been measured. The second wave of the smoking ban came into effect in January 2008, extending it to public places such as cafes, restaurants, nightclubs and casinos. Again, implementation should be fast and face little resistance, as 80% of the French population (including 60%–65% of smokers) support smoke-free public places and workplaces (INPES 2007).

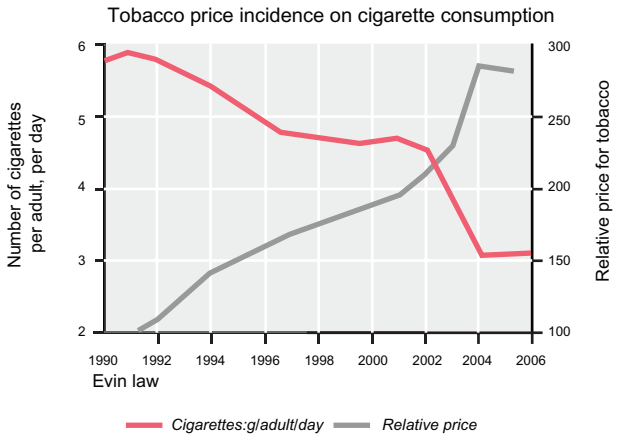

Figure 4 Effect of cigarette price increase on consumption among French adult smokers between 1990 and 2006 (produced by Catherine Hill, Epidemiologist, Gustave-Roussy Institute, Villejuif Cedex, France).

Despite these positive steps, the tobacco industry continues apace and the money generated through tobacco taxation remains high. In 2007, the price of a pack of cigarettes was approximately €5.3. With 80.4% of this price levied by taxes and the number of French smokers estimated at approximately 11.7 million, it is understandable how the Government managed to collect €11.8 billion of tax through tobacco products in 2006. Also in that year, an estimated 65,700 tonnes of tobacco were sold (including 55,800 tonnes

Table 3 Number of deaths attributable to smoking in France 1999 (Hill and Laplanche 2003)

Causes of death	Men	Women
Cancers	32,000	2,500
Cardiovascular diseases	10,500	1,400
Respiratory diseases	8,300	1,300
Others	8,300	1,300
Total	59,000	7,400

of cigarettes), reaching levels equivalent to those of 2004 and 2005 because of the 2003 "armistice" that prevented tax increases for 4 years. Furthermore, the legal cross-border market is estimated to have grown from 8,600 tonnes in 2004 to 9,900 tonnes in 2005. Of concern for anti-tobacco groups in the UK, French Customs agents seized 240 tonnes of tobacco (47 tonnes of counterfeit cigarettes) in 2006 that were largely en route to the UK, where cigarette prices are higher (INPES 2007).

At the 1997 World Tobacco or Health meeting in Beijing, Richard Peto reported that 520 million smokers had died or would die between 1950 and 2050 (Peto et al 1999). Even if primary prevention goals were achieved, which would halve the prevalence of smoking among the young, he argued that 500 million would still die. Yet, according to Professor Peto's figures, if the smoking prevalence among adult smokers could be halved before 2020, the total number of deaths could potentially be reduced to 320 million.

Pharmacological aids to smoking cessation

Pharmacological options with proven efficacy for smoking cessation first appeared on the French market around 2 decades ago. The first was NRT, followed nearly 10 years later by sustained-release bupropion and then, in February 2007, by varenicline. Both NRT and sustained-release bupropion have been shown to double the chance of successful smoking cessation (Stead et al 2008), whereas clinical trials have found varenicline triples the likelihood of a successful quit attempt (Cahill et al 2007). In addition to the proven pharmacological efficacy of such agents, smoking cessation agents need to be widely available, accessible and affordable to stand a chance of offering real benefits to smokers attempting to quit.

NRT and bupropion

Despite concerted efforts between 1999 and 2002 to increase their frequency, the number of smoking clinics in France remains rather low. NRT lacks credibility in the medical community and the need for a medical prescription has served as a barrier to its use, fuelling arguments for making it available OTC (Dubois 1999). OTC availability of NRT in the rest of the world has doubled its use and its efficacy has been demonstrated in the real world, beyond the controlled parameters of trials (West 2007).

NRT is licensed in France for temporary abstinence in patients over the age of 15 years (including pregnant women). It is legal to advertise NRT through the media (including television advertising) and all forms are available; furthermore, combinations are also authorized. Contraindications to NRT have generally been suppressed. As previously stated, sustained-release bupropion is also available on the French market, but its use is decreasing rapidly.

Varenicline

Conversely, varenicline, which became available in France by prescription in February 2007, has been widely used in its first year. The agent's introduction to the market coincided with the implementation of the workplace smoking ban. So far, varenicline appears to have been well received and well perceived by GPs and specialists, despite warnings of possible related depression and suicide (FDA 2007). These warnings have had little impact on the attitudes of French clinicians towards the agent. Similar concerns have been raised with all types of pharmacological treatment aids for smoking cessation, and it is largely believed that such feelings are more likely linked to the act of cessation rather than to the treatment.

Smoking cessation as a health intervention

Smoking cessation is one of the most cost-effective healthcare interventions available (US Surgeon General 2000). Nevertheless, reimbursement of products that support smoking cessation has been long debated in France, despite the strong support and campaigning of the Alliance. Following applications for reimbursement to be considered for pregnant women and those people with conditions that are aggravated by smoking, it was agreed that normal reimbursement of prescribed pharmacological treatment for tobacco dependence would be supported. Yet, the report published by the High Health Authority in France in January 2007 (HAS 2007) favored a payment model and the government has ruled to subsidize prescribed treatment only up to a maximum of €50 annually.

Following the various national anti-smoking initiatives in France (including the workplace smoking ban, introduction of varenicline, and subsidizing of pharmacological treatment for tobacco dependence), the French monitoring center for Drugs and Drug Addiction (Observatoire Français des Drogues et des Toxicomanies [OFDT]), reported an increase of 60% in sales of smoking cessation products during the first trimester of 2007 compared with the same period of 2006 (OFDT 2008). The OFDT also reported that over the same period, use of smoking clinics increased by a quarter and prescriptions were subsidized for 42,600 patients (totalling €1.6 million).

OFDT reports a 1.3% drop in the cigarette market over the first 11 months of 2007, and a decrease in the self-rolled cigarette market of 1.2% (OFDT 2008). The mean number of new patients in smoking clinics during the first 11 months of 2007 increased by 5.6% (resulting in the delay for an appointment lengthening from a mean 11 to 20 days). In addition, the tobacco dependence treatment market increased by 33%, to over 2 million months of treatment. This growth comprised: a 7.8% increase for transdermal NRT (839,781 months of treatment); a 14.3% increase for oral NRT (772,779 months of treatment); a 43.5% decrease in the use of sustained-release bupropion (54,600 months of treatment), and a high use of the newly available varenicline – with a total of 390,415 months of treatment having been prescribed during this period (and 45,976 months prescribed during November alone). The significant use of smoking cessation products by French patients resulted in the maximum €50 being paid 388,488 times by the French NHS (OFDT 2008). Currently, the varenicline market in France is estimated to be worth around €50 million, which compares with an estimated €100–110 million for the NRT market.

Conclusions

Legislation on tobacco use in France first came into force in 1976. In compliance with the WHO FCTC, existing legislation: regulates levels of tobacco taxation; (essentially) bans tobacco advertising; prohibits smoking in public places; targets tobacco smuggling; bans the sale of tobacco to minors (those aged less than 16 years); promotes large anti-tobacco media campaigns and improves availability and affordability of pharmacological treatments for tobacco dependence. The country's proactive approach to targeting tobacco dependence has been driven by the NGOs (working under the umbrella of the French Alliance against Tobacco) and their close work with the media, the government and members of Parliament. Since 1991, the number of cigarettes smoked per adult has reduced by 50% (see Figure 4) and, with the aid of new legislation and tobacco dependence products, the benefits of smoking cessation as an effective healthcare intervention should soon be realized.

The Norwegian perspective

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Introduction

The Norwegian Health Authorities have been rather aggressive in their introduction of nicotine advertising bans and, more recently, smoking bans. Contrastingly, they have been less proactive in their efforts to support smoking cessation. An example of this poor support is the fact that, although varenicline seems to have been well received in Norway, realization of its optimum utility has been hampered by a lack of reimbursement.

National smoking prevalence

Nearly a quarter of Norway's adult population smoke on a daily basis. This number has been in steady decline for more than 30 years, dropping rapidly over the last decade (from 33% in 1998 to 22% in 2007). The male (21%) and female (23%) prevalence is evenly weighted, and has been so for the last few years (Directorate for Health and Social Affairs 2008) (see Figure 5).

Promisingly, the prevalence of daily smokers among youths (aged 16–24 years) has declined from 24% to 16% between 2005 and 2007. A positive trend can also be seen among younger teenagers (aged 13–15 years) in whom surveys report there has been a decline from 10% to 5% between 2000 and 2005. It is not yet known whether this trend will continue, but policies are being put in place to half the 2005 daily smoking prevalence of 24% among young people (aged 16–24 years) by 2010 (Directorate for Health and Social Affairs 2008).

Smoking-related health burden

The burden of smoking-related diseases in Norway is growing, especially among women. In 2004, the female mortality rates for lung and larynx cancer exceeded that of breast cancer. Twenty-five years ago, the prevalence of lung cancer among men was 4 times that among women; today this has halved with the male prevalence only twice that seen for women. In fact, in patients less than 50 years of age, there are now more cases of lung cancer registered for women than there are for men. The increase in the incidence of lung cancer among women is closely correlated to the increased smoking prevalence among the female Norwegian population over the last

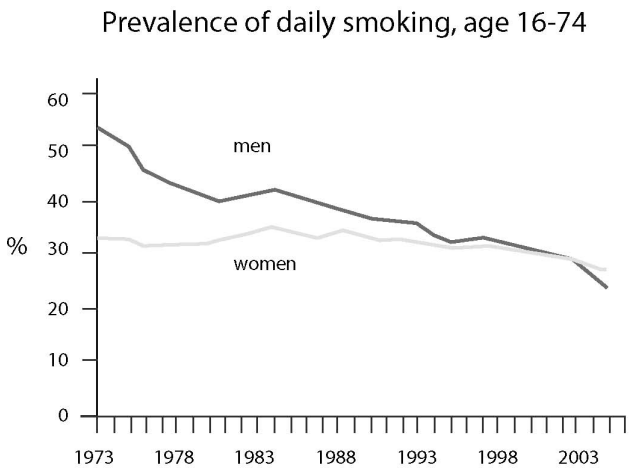

Figure 5 Prevalence of daily smoking among the Norwegian population (aged 16–74 years) between 1973 and 2004 (Directorate for Health and Social Affairs 2008).

few decades (Directorate for Health and Social Affairs 2004). In addition, although there are no accurate data recording the prevalence of chronic obstructive pulmonary disease (COPD) and its related mortality in Norway, the numbers are rising and COPD patients represent a growing challenge to the nation's hospitals (Directorate for Health and Social Affairs 2004). As is the case in most Western countries, cardiovascular mortality in Norway is declining, yet cardiovascular diseases are the greatest cause of increased mortality among smokers, leading to more than 4,000 deaths every year (Directorate for Health and Social Affairs 2008).

Policy and attitudes towards smoking cessation

Norway was one of the first countries to sanction a Tobacco Act. The Act, sanctioned in 1973, came into force in 1975. It banned tobacco advertising, legislated tobacco labeling, and prohibited children younger than 16 years from buying tobacco products. The legal age for buying tobacco products was increased to 18 years in 1996. In addition, the country adopted The Clean Air Act in 1988, which ensured smoke-free air in public localities and on public transportation. A total ban on smoking in all public places, including restaurants and bars, has been in effect since 1 June 2004.

When the total ban first came into force in 2004, it had the support of just over half of the population (54%). Since that time, public support has increased dramatically, rising to 85% by June 2007. Unsurprisingly, public support is higher among non-smokers than among smokers, but even among daily smokers, approximately 60% report positive attitudes towards smoke-free bars and restaurants.

Positive attitudes towards smoking cessation are supported by the health authorities' annual, national mass media campaigns to educate on tobacco and health, and by national guidelines that were developed and distributed to GPs in 2004 to advise on smoking cessation in primary care. In addition, the government hosts a national quit line with a toll free number to support those attempting to give up smoking, and offers training to group leaders from around the country to assist them in running their smoking cessation meetings.

Despite these encouraging steps, smoking cessation is not part of the curriculum for medical students or other health personnel, and there are still no smoking cessation clinics in Norway at the time of writing.

Varenicline in clinical practice

Since its introduction to the Norwegian market in December 2006, varenicline has been well received by both physicians and the public.

Before the introduction of varenicline, bupropion was the only nicotine-free medication available to assist those trying to give up tobacco products, but it had a somewhat negative reputation after media coverage of related side effects. So far, varenicline has escaped a similar fate, and general impressions among patients and health professionals are that its side effects tend to be mild. Associated nausea is the main area of concern, but this can be reduced by taking the tablets with food. From experience, most patients are able to tolerate the nausea, but for those more severely affected, it may be helpful to suggest they take the first dose at lunch rather than in the morning, or to reduce the dose.

Among physicians, varenicline seems to have established itself as the most effective medication available for smoking cessation. Yet NRT remains by far the most-used pharmacological support by smokers trying to quit. This is likely because varenicline must be prescribed by a physician, in contrast to NRT, which is much more accessible and can be purchased OTC (even in food stores). Its ease of access results in smokers tending to use NRT at their own convenience, and the results are probably much less favorable than the clinical studies would foretell.

The main aims to achieving optimum smoking cessation outcomes in Norway at this time are:

- to educate smokers of the importance of seeing their physician when considering quitting, and the beneficial effect it can have on quit rates as compared with unsupported quit attempts,
- to endeavor to engage every GP as a smoking cessation agent,

- to provide follow-up care with behavioral support and counseling (eg, from a trained nurse) for smokers attempting to quit,
- to help motivate patients who are prescribed varenicline to continue the treatment for at least 12 weeks.

Smoking cessation challenges

A further example of the health authorities' less than robust support for smoking cessation is the absence of reimbursement for smoking cessation medication in Norway. Cigarettes are expensive due to high taxes and the cost of varenicline treatment can be equated to the cost of smoking approximately 7–8 cigarettes a day. While most smokers might feel that this is affordable, some may still give up treatment with varenicline before completing the recommended 12-week period, which inevitably results in poorer treatment outcomes and effectiveness. Provision of reimbursement would probably help more smokers to finish the full treatment course as prescribed.

This argument is particularly true when the social inequality associated with smoking is taken into consideration. Smoking rates are correlated to socioeconomic factors, with high smoking rates being found among those with low levels of education and income. Fixing a high price for smoking cessation medication will result in a perpetuation of such social inequality in health. The Norwegian government has defined social inequality in health as one of the key challenges of modern times, so it can only be hoped that reimbursement will soon be provided for medicines that reduce the divide, including those for smoking cessation. Luk Joossens and Martin Raw recently published their survey of tobacco control activities across 30 European countries (Joossens and Raw 2007). Norway ranked number 4 on their list in 2007, having scored 66 out of a possible 100 points. This finding confirms that Norway scores highly when it comes to restrictive tobacco policies, but it would score less well on a similar survey designed to assess support for smoking cessation. At this time, the Norwegian government legislates well, but simply does not spend enough money (as a proportion of Gross Domestic Product) to support tobacco control activities.

The Polish perspective

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National prevalence and burden of smoking

A substantial reduction in Poland's smoking prevalence has been seen over the last 25 years. This is particularly true for men, in whom the proportion of smokers continues to decline. In the early 1980s, almost 60% of adult men in Poland smoked, whereas by 2006 the number had decreased to 37% (WHO 2007b). The degree of decline is less evident among female smokers over the same period. There has been almost no change in the smoking rates among Polish women in the last decade, with 23% of women continuing to smoke in 2006 (WHO 2007b). It appears that most smokers in Poland begin smoking before the age of 18 years. Moreover, approximately 70% of children aged 12 years admit to having had contact with tobacco (Mazur et al 1999).

National prevalence hides a significant regional variation in smoking rates, according to the Polish National Health Survey, Project WOBASZ (Polakowska et al 2005). The variation among men aged 20–74 years ranged from 48% in the northeastern region of Poland to 34% in the south. Even greater regional differences were found in women, with the highest prevalence of 34% again reported in northeastern Poland and the lowest rate of 15% recorded among women living in the southeast of the country. The survey also found that the volume of cigarettes consumed by smokers in Poland is high, with men smoking an average of 18 cigarettes a day and women an average of 14 cigarettes a day (Polakowska et al 2005).

Another important contributor to the health burden is the prevalence of smoking among those already living with smoking-related diseases, such as ischemic heart disease. The Cracovian Program for Secondary Prevention of Ischemic Heart Disease assessed patients hospitalized due to ischemic heart disease and found that, of those patients who smoked in the month prior to their hospital admission, nearly half still smoked one year later (Jankowski et al 2003). Recently, additional (unpublished) data suggest that this is a continuing problem; indeed, it suggests that approximately 18%–20% of high-risk patients in

Poland smoke and that this percentage has not changed significantly over the last 10 years (Jankowski et al 2003).

Over the last 20 years, the age-standardized cardiovascular mortality rate in Poland has been reduced by almost 40% (for both men and women) (see Figures 6 and 7). Particularly significant reductions have been observed for premature cardiovascular death (in patients below the age of 65 years). In addition to the implementation of appropriate lifestyle changes and better management of cardiovascular risk factors, reduced smoking rates may have contributed to this reduction in mortality.

A downward trend in prevalence has also been observed in the rate of malignant neoplasms among young men over recent years (see Figures 8 and 9). Similarly, a reduction in lung cancer mortality can also be seen among young men. By contrast, lung cancer mortality has actually increased among women and older men. The increase in lung cancer mortality among women compared to the reduction seen among the young male population may be a result of the aforementioned contrasts in smoking prevalence trends among women and men in Poland over last 30 years.

The reduction in lung cancer mortality among men was first observed after the collapse of communism in Poland, an event that was associated with rapid and profound economic, political and social reform. Data from the WHO's European health for all database suggest that similar trends can be seen in most Central European countries and that these social transformations may positively influence both cancer and cardiovascular mortality rates (WHO 2007b).

National policy and attitudes towards smoking

In Poland, NRT is available over the counter, while bupropion and varenicline are available by prescription only.

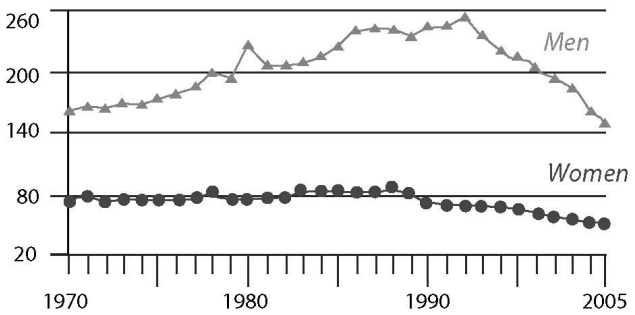

Figure 6 Age-standardized cardiovascular mortality (per 100,000) in Polish men and women aged less than 65 years (WHO 2007b).

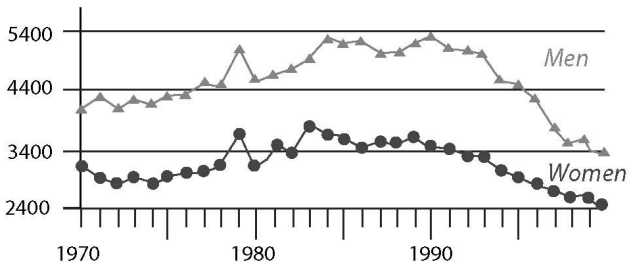

Figure 7 Age-standardized cardiovascular mortality (per 100,000) in Polish men and women aged over 65 years (WHO 2007b).

Although a number of grassroots initiatives in smoking cessation have been launched in Poland in recent years, there has been a lack of formal and financial support from the State or the Polish NHS. Effective management of smoking is one of the most cost-effective health interventions available in modern medicine. In light of the effectiveness of smoking cessation, the cost of pharmacotherapy to aid cessation should be at least partially reimbursed by the State. Unfortunately, this is not the case in Poland, where the only smoking cessation costs that have been met by the NHS and industry are those of small initiatives. Recently, the Polish Forum for Prevention of Cardiovascular Diseases (an important Polish collaboration of several scientific societies) has called for the wider reimbursement of smoking cessation therapy (Kawecka-Jaszcz et al 2008). Whether the desired funding from the Polish Government transpires or not will become clear in the near future.

Recent research suggests rather infrequent use of pharmacotherapy for smoking cessation (both NRT and oral therapies) in Poland at this time. One reason for the low use of pharmacological smoking cessation aids could be the lack of reimbursement, but another could arguably be a lack of adequate medical care, which has been indicated as a major problem in most developed countries (Anonymous 1996; Stamos et al 2001; Hoch et al 2004). This treatment gap in smoking cessation has been attributed to a number of factors, including: time constraints; lack of incentives, resources, and facilities; inadequate communication between primary and secondary care providers; and a focus by physicians on more acute health problems (Anonymous 1996). Given the low use of pharmacological smoking cessation aids, it is perhaps surprising that most Polish physicians claim to take an aggressive approach to treating risk factors (Stamos et al 2001; Heilmann 2007). As the WOBASZ National Health Survey found that the vast majority of smokers in Poland (over 80%) claim that

they would like to give up smoking (Polakowska et al 2005), it appears that there is a huge (currently untapped) potential for healthcare providers. It may be that interventions aimed at physicians and other healthcare providers are required in this area, in addition to those aimed at the patient.

The health consequences of passive smoking (constrained exposure to tobacco smoke) are not significantly different to those resulting from active smoking. It is important in Poland, therefore, to improve protection for non-smokers against the harmful effects of second-hand smoke in public places. The benefit of smoke-free public environments on national tobacco-related morbidity seen in other European territories (Barone-Adesi et al 2006; Bartecchi et al 2006) paves the way for establishing similar smoking bans in public places (eg, prohibition of smoking in public workplaces, on public transport, and in bars and restaurants) in Poland.

The legislation in Poland lags behind that of many European countries. Nonetheless, smoking is forbidden in schools, hospitals, and workplaces, and is restricted to allocated rooms in bars and restaurants. It is also forbidden on airplanes and at train stations, although allowed on trains within segregated areas. Some cities in Poland have also introduced smoking bans in parks and playgrounds, and at bus/tram stops, but compliance with these initiatives tends to be poor. Several attempts have been made to introduce a national ban in all public places, but the legislation seems to fall down before the final vote in Parliament. Although more than 75% of adults in Poland support the introduction of such a ban, and Parliament would likely pass a bill were it given the chance to vote, there remain some powerful lobbyists in the smoking camp. The fact that some of the influential public health politicians in Poland are smokers, and that the new Polish Minister of Health opposes the ban (Polish Forum for Prevention of Cardiovascular Diseases 2008), may also explain some of the resistance. In addition, there is resistance from smokers themselves on the premise that a ban compromises their freedom of choice, albeit with the aim of protecting non-smokers from the potential health implications of that freedom. At the time of writing, the Polish Forum for Prevention of Cardiovascular Diseases had recently called for an improvement in levels of protection for non-smokers from the harmful effects of second-hand smoke in public places (Kawecka-Jaszcz et al 2008).

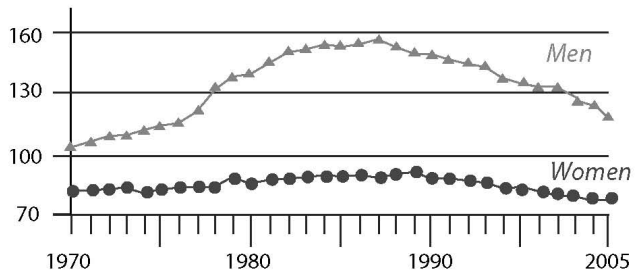

Figure 8 Age-standardized mortality due to malignant neoplasms (per 100,000) in Polish men and women aged less than 65 years (WHO 2007b).

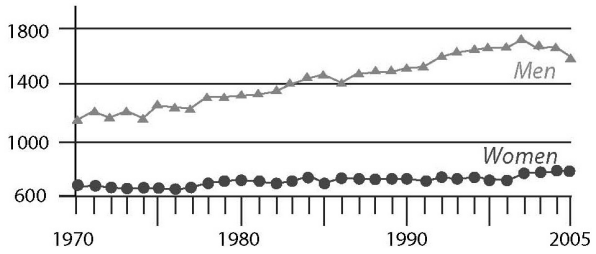

Figure 9 Age-standardized mortality due to malignant neoplasms (per 100,000) in Polish men and women aged over 65 years (WHO 2007b).

A new option in smoking cessation

Varenicline is the newest pharmacological treatment option available to aid smoking cessation. The agent was launched in Poland in 2007 and, despite its relatively short period of use in clinical practice, first impressions among physicians are very positive. It appears to be as effective in the real-world setting and in real patients as the large-scale randomized clinical trial data suggest; it also seems to be relatively well tolerated.

My own clinical experience also indicates that varenicline may be effective and well tolerated in patients with heart disease, although so far no studies specific to this patient group have been carried out. In my own experience, I have also used varenicline in patients with acute heart disease. The psychological momentum towards quitting smoking is particularly strong at the time patients are diagnosed with a smoking-related condition and when they are informed of a need for invasive treatment as a result of their condition. This strength of feeling should be capitalized on and such opportunities to promote smoking cessation interventions should not be overlooked. With this in mind, the formal assessment of the safety and efficacy of varenicline in patients who have recently experienced an acute smoking-related event would be of great value. Further data from specifically designed clinical trials in this area would help to inform clinical practice in the future.

Conclusions: new lessons learned in smoking cessation

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The role of varenicline

This review of clinical experience with varenicline, pooled from across Europe, supports varenicline's strong efficacy trial data in clinical practice and reflects the positive reception it has received across the continent.

According to our experience, the agent's main role might be in assisting moderate or heavily dependent smokers and smokers who have tried and failed to quit smoking, in renewed attempts to break their tobacco dependence. Varenicline may also have a role in assisting: smokers who have never tried to stop because they simply cannot imagine that they could successfully quit; those with a persistent dependence on nicotine (from NRT) and (arguably) those patients who express a preference for varenicline.

Dr Jankowski makes the important clinical point that the momentum to quit smoking tends to be greatest when patients are first diagnosed with a smoking-related disease, or when they are informed of a need for invasive treatment as a result of their smoking-related condition. It is important for clinicians to seize these opportune moments to promote smoking cessation in patients. Further clinical trials with varenicline in patients who have suffered a smoking-related event would help inform clinical practice in this area.

Elements of successful smoking cessation programs

The papers contained within this supplement bring together different experiences in smoking cessation from across Europe. With a view to utilizing some of the lessons learned and refining clinical practice as appropriate, what follows is a short summary of our own experience, although it is by no means an exhaustive list.

Regulation

Prof. Dubois' review of French tobacco legislation highlights the importance of national legislation that minimizes tobacco abuse. The significant reduction in smoking seen in France between 1991 and the present day is proof of the effectiveness of legislation that regulates product promotion and availability and introduces bans in public places. In particular, legislation can help to change the public's perception of smoking, forcing a revision of general attitudes and levels of acceptance. Professor Dubois' article recognizes the role NGOs have played in raising the public consciousness in France and in campaigning on a political level.

After adopting the appropriate legislation, there is also a need for healthcare professionals to offer support to smokers who are motivated to quit smoking. As Dr Gronert states in his review of the Norwegian situation, the Norwegian government legislates well but it has been less proactive in supporting smoking cessation.

Patient education

While some smokers may be well aware of the health risks associated with their dependence on tobacco, many remain ignorant of the implications of their habit. Even those who do understand the potential effects smoking can have on their health often fail to realize that their dependence is a disease. They may also lack knowledge of the existing treatment options. As such, education is the first step towards motivating a desire and willingness to quit among smokers. It can be helpful to explain nicotine's mode of action to patients: how it acts on the dopamine receptors in the brain in a way that affects their mood and leads to a dependency on the drug. An explanation of the underlying processes at work helps to clarify in the smoker's mind the principle of physical dependence. From my own clinical experience, I believe that this type of education can help reassure patients that smoking is more than just a bad habit. It can also help them to understand why they may have experienced difficulties with quitting previously, while at the same time giving them some insight into how medication can act on the physical dependence and play a role in successful cessation.

In addition to explaining the underlying addiction to nicotine to smokers, it is important to initiate a discussion about the available treatment options (how they work; their potential side effects) and their benefit in quit attempts. In the case of varenicline, it can be beneficial to explain the dual

mode of action: it should minimize any reward they usually experience from smoking, while at the same time reducing their desire to smoke. Part of the treatment education process is the management of any unrealistic expectations patients may have. It must be enforced that neither varenicline nor other smoking cessation therapies are "miracle pills"; treatment alone is certain to result in a failed quit attempt. Smoking cessation products have a realistic chance of success only when taken by patients who genuinely want to give up smoking. Varenicline is not a smoking "cure", but it is a useful aid to achieving abstinence when taken by patients with commitment and strong will power who are willing to implement the necessary lifestyle changes.

In addition to managing patients' expectations, it is also crucial to educate patients on the importance of continuing with therapy for the prescribed period. Dr Vanuzzo reviewed the results of an Italian study that reported 60% compliance for the full duration of treatment, and found that the main reason for non-compliance was self-medication by patients who believed they were already "cured". Side effects can be another reason for early discontinuation of treatment. In the case of varenicline, it is pertinent to warn patients of possible nausea, but also to explain that it tends to pass as treatment continues. If they do experience nausea, it is beneficial to offer advice as to how it can be minimized (some suggestions follow shortly). It can also be useful to refer patients to varenicline's prescribing information and to talk them through the possible adverse events, taking time to differentiate between agent-related side effects and those likely resulting from nicotine withdrawal itself.

Physician education

Even physicians continue to consider smoking a bad habit rather than a disease, particularly in Eastern Europe. Physicians need to understand that tobacco dependence causes diseases that affect all areas of medicine and thus, they should actively promote intervention and treatment of tobacco dependence.

As Dr Raupach's contribution from Germany highlighted, there is not only a need to educate patients about the various smoking interventions and smoking cessation treatments available, but also a need for better physician training. This is a sentiment that was reiterated by Dr Jankowski in his Polish review. While the German data indicate that primary care physicians believe they play an important role in smoking cessation promotion (Heilmann 2007), smoking status is not routinely assessed in the primary care setting, and cessation advice is only offered to 40%–65% of all smoking patients (Hoch et al 2004). Dr Raupach suggests that this may be caused by a lack of confidence among GPs as to what advice they should offer smokers who are attempting quit. This theory is supported by a survey carried out among 315 German GPs, which found that two-thirds rated their training as inadequate (Twardella and Brenner 2005). Dr Raupach's data also reported a significantly higher quit rate in patients receiving smoking cessation pharmacotherapy in conjunction with group counseling, highlighting the improved cessation rates achievable if appropriate agents are used.

Physician education should be ongoing and healthcare professionals should remain up-to-date with license changes and results of post-marketing surveillance studies. Adequate education will enable physicians to accept concerning developments – such as reports of depression and suicidal ideation in patients receiving tobacco dependence treatment – in a considered way, and to understand that such events are more likely related to smoking-withdrawal symptoms than to the treatment itself. The Food and Drug Administration (FDA) in the US is currently investigating reports of depression and suicide related to varenicline treatment; however, Prof. Dubois tells us that such warnings have had little impact on the attitudes of French clinicians towards the agent because of similar such concerns having been raised with all types of pharmacological aids in tobacco cessation. His opinion is that such feelings are more likely linked to the act of cessation rather than the treatment itself. Clinical experience and continued education will help physicians prescribing varenicline to make their own, informed decisions on this issue and future developments with the agent.

Below are some practical suggestions (drawn from the experiences of my co-authors, my patients and my own clinical practice) that may be of use for patients prescribed varenicline.

Dealing with adverse events

Although many patients will experience no adverse events associated with their varenicline treatment, up to 30% may report nausea, which, although it is inconvenient, is not dangerous. The nausea usually subsides within a few days, but some simple advice on how best to take the medication can minimize such experiences. Insights gained from my own patients suggest the following may help to reduce symptoms of nausea:

- taking the medication after/during a meal,
- drinking water (up to two glasses) when taking the medication,
- remaining on a dosage of 0.5 mg rather than titrating up to the 1.0 mg, if the nausea persists,

- moving the time of treatment administration from first thing in the morning to around 11 am, after eating a snack,
- lying down for 10 minutes after taking the treatment,
- chewing gum after swallowing the tablet.

Quitting: D-day

Ideally, the quit date for patients taking varenicline occurs during the second week of treatment, preferably day 8 of treatment, at which time the effects of varenicline should be apparent and patients should feel a reduced urge to smoke, or (if they do smoke) should find that the pleasure of smoking has diminished. However, the patient should decide the exact quit date that is most suitable for them. If they choose a date slightly later in the treatment course, it need not be problematic. An important requirement of remaining on medication is a patient's willingness to quit. If a patient has failed to quit over the course of the 3-month treatment period, but reports a loss of desire to smoke (varenicline's agonistic activity) and no reward after smoking a cigarette (varenicline's antagonistic activity) treatment continuation would be recommended at our clinic.

Duration of treatment

Varenicline is licensed for a treatment duration of at least three months, with the possibility of continuing therapy for a second 3-month period in patients who have quit but may benefit from an additional course (eg, in those who have only recently managed to quit.) As I discussed in the introduction, there is evidence to suggest that extending the treatment duration to six months can significantly increase the quit rate when compared with three months of treatment (Tonstad et al 2006). The potential benefit of continuing treatment for an additional three months must be weighted against the already-prescribed cost of treatment and the cost of extending therapy. However, given the money already spent on treatment, it may be a false economy to cease therapy before abstinence has been achieved if prolonging therapy is likely to result in successful cessation. It is at the discretion of clinician to judge whether the additional treatment period is justifiable and indeed necessary.

It is my opinion that, as a chronic, relapsing disease (like hypertension), tobacco dependence requires treatment over a long term. With this in mind, I would recommend that long-term smoking cessation pharmacotherapy (be it NRT, bupropion or varenicline) may increase the quit success rate in clinical practice. In the case of varenicline, if patients report a reduction in their desire to smoke and a loss of smoking enjoyment, but have been unable to achieve full abstinence after three months (eg, extremely heavily smokers who have reduced their daily cigarette use from 40–80 a day to 2–5 a day), I would recommend a continuation of varenicline therapy. In heavily dependent smokers, my recommendation may even be to continue treatment beyond six months. Abstinence is the target, but it should be recognized that patients reach different stages of their treatment at different times and that some patients reduce their usage with the aim of stopping rather than quitting abruptly.

Reimbursement

Although smoking cessation is one of the most cost-effective healthcare interventions available, reimbursement of varenicline by the respective national health services discussed in this supplement remains partial or non-existent.

In France, the issue of reimbursement has long been debated and there is currently a €50 cap on reimbursement. The high level of demand is evident, however, through Prof. Dubois' report that in the first 11 months of 2007, the French monitoring center for Drugs and Drug Addiction (Observatoire Français des Drogues et des Toxicomanies [OFDT]) recorded a growth in the tobacco dependence treatment market of 33% and the maximum €50 reimbursements being paid by the National Health Service 338,488 times (OFDT 2008).

From my own experience in the Czech Republic, most health insurance companies reimburse only around two weeks of treatment (up to €40), but this remains better than the approach seen in other European countries. Norway, Italy, Germany and Poland currently offer no standard reimbursement at all, despite public and physician opinion and pressure advocating for national funding of smoking interventions.

As Dr Raupach and Dr Gronert rightly highlighted, the cost of smoking cessation medication is especially relevant among lower socioeconomic groups – the groups in whom smoking prevalence is highest. Although Dr Gronert's financial analysis suggests that in Norway, high tobacco taxation means that the cost of varenicline treatment can be equated to the cost of smoking only 7–8 cigarettes a day, treatment cost and lack of reimbursement remain a substantial barrier to treatment compliance. Cost issues are likely to affect compliance with varenicline for the duration of the recommended 12-week treatment period, not to mention treatment beyond that for which higher success rates could possibly be achieved (Tonstad et al 2006). In theory, reimbursement

of medication costs could result in improved success rates among quitters (Fiore et al 2008).

Conclusions

Although it is still early days since varenicline was launched, pooled clinical experience from around Europe indicate that it is not only very positively perceived, but also as effective as the early randomized controlled trial data suggest. It may not be a "miracle pill" that hopeful quitters seek, but it significantly increases the chance of successful quit attempts in motivated smokers when compared with placebo and other smoking cessation products. It may be a particularly useful aid for heavier smokers with a greater dependence on nicotine. In addition, education among physicians of the agents' dual mode of action serves as a reminder to physicians and their patients that tobacco dependence is recognized as a valid medical condition.

Reimbursement remains an obstacle for optimal utilization of varenicline and other smoking cessation aids, despite the relatively low cost of treatment when compared with the cost of habitual smoking (ie, the cost of varenicline treatment is equivalent to approximately 7–8 cigarettes a day in Norway, and at least 20 cigarettes a day in the Czech Republic). Unfortunately, trends in smoking prevalence indicate that the highest rates of smoking exist among patients who are least able to afford treatment. In time, pressure from the public, healthcare professionals and NGOs, coupled with changes in mindset brought about by increasing anti-tobacco legislation, may work to change national policies on reimbursement. Funding requirements may be overshadowed by those of treatment for acute conditions, but as one of the most cost-effective healthcare treatments, support for smoking cessation should be prioritized.

On a more personal note, since using varenicline in clinical practice, I have received feedback from patients who have successfully achieved abstinence after many years of trying to quit smoking. They have spoken of the "freedom" they now feel following years of "tobacco slavery". As a clinician, it is a pleasure to hear such comments.

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