Does over-the-counter nicotine replacement therapy improve smokers' life expectancy?

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Abstract

Objective—To determine the public health benefits of making nicotine replacement therapy available without prescription, in terms of number of quitters and life expectancy.

Design—A decision-analytic model was developed to compare the policy of over-the-counter (OTC) availability of nicotine replacement therapy with that of prescription (℞) availability for the adult smoking population in the United States.

Main outcome measures—Long-term (six-month) quit rates, life expectancy, and smoking attributable mortality (SAM) rates.

Results—OTC availability of nicotine replacement therapy would result in 91 151 additional successful quitters over a six-month period, and a cumulative total of approximately 1.7 million additional quitters over 25 years. All-cause SAM would decrease by 348 deaths per year and 2940 deaths per year at six months and five years, respectively. Relative to ℞ nicotine replacement therapy availability, OTC availability would result in an average gain in life expectancy across the entire adult smoking population of 0.196 years per smoker. In sensitivity analyses, the benefits of OTC availability were evident across a wide range of changes in baseline parameters.

Conclusions—Compared with ℞ availability of nicotine replacement therapy, OTC availability would result in more successful quitters, fewer smoking-attributable deaths, and increased life expectancy for current smokers.

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Introduction

Smoking cessation and prevention strategies hold tremendous potential to improve public health.[1] Smoking-attributable mortality is now estimated at more than 400 000 deaths per year and the health benefits of quitting at any age have been well documented.[2] Although over 70% of smokers would like to quit smoking,[3] less than 5% of self-quitters successfully stop smoking for six months or more,[4] a figure considerably lower than the 10–30% quit rates produced by smoking cessation programmes using prescription (℞) nicotine replacement products (transdermal patches or polacrilex gum).[5–7] Although smoking cessation programmes are more efficacious than self-quitting, considerable evidence suggests that most smokers are reluctant to participate in cessation programmes.[8–10] This suggests that making nicotine replacement products available outside formal cessation programmes may increase smoking cessation rates among American smokers. One strategy to make nicotine replacement products more available to self-quitters is to make them available over the counter (OTC).[11 12]

In July 1996, the FDA first approved over-the-counter sales of one brand of nicotine patch.[13] The patches appear to be a popular cessation aid; by the end of 1996, one brand of OTC nicotine patch, Nicoderm CQ, had sold over 3.2 million units (unpublished data, SmithKline Beecham, Inc.). Use of nicotine replacement therapy has been estimated to increase by over 150% since nicotine patches and nicotine gum have become available without prescription.[14] An accurate estimate of the potential public health benefits of the policy of making nicotine replacement available without prescription depends upon formal analysis that models the anticipated benefit based upon specific, empirically derived assumptions. The current study used decision-analytic techniques to compare the public health impact of prescription with over-the-counter nicotine replacement therapy availability. The analyses used data on the estimated percentage of American smokers who would quit successfully per year, and on estimated reductions in smoking-attributable mortality, derived from sources available before nicotine replacement was available OTC in the United States, or from post-marketing surveillance after nicotine replacement was available without prescription.

Methods

We constructed a simulation model[15] using a computer spreadsheet (Microsoft Excel for Windows version 5.0, Microsoft Corporation, Redmond, Washington) to compare the public health impact of making nicotine replacement therapy (NRT) by transdermal patch or by nicotine polacrilex gum available over the counter (OTC scenario) with the practice of prescription-only availability (℞ scenario). We used data from non-prescription availability Nicoderm patch studies conducted by Alza Corporation as proxy for over-the-counter nicotine replacement in general, due to the availability of over-the-counter data for this particular product. Outcomes determined for

Table 1 Model parameters

Parameter	Value*	Sources
OTC scenario		
Probability of using NRT if attempting to quit	0.35	8, 14
Probability of quitting six months using NRT†	0.106	19
℞ Scenario		
Probability of using NRT if attempting to quit	0.14	8‡
Probability of quitting six months using NRT†	0.106	19
Both scenarios		
Probability of attempting to quit by any method	0.31	17§
Probability of quitting six months for those attempting without NRT†	0.049	4, 24
Markov models		
One-year probability of relapse for quitters in first two years	0.11	2¶
One-year probability of relapse for long-term quitters	0.024	2¶
Relative risk of death, current smoker to former smoker (age 18–29 years)	1.0	**
Relative risk of death for current smoker to former smoker (age ≥30 years)	Age and sex dependent (range: 1.2–2.5)	1, 17, 23††
One-year probability of death, former smoker	Age and sex dependent (range: 0.0051–0.18)	16

OTC = over the counter; NRT = nicotine replacement therapy.
*Values for table 1 are presented as the weighted average of values across age and sex strata.
†Based on self-reported continuous quit rates in OTC setting; see text.
‡Based on all reported NRT use (patch and gum) from Pierce *et al.*[8]
§Based on the 1992 National Health Interview Survey data from the National Center for Health Statistics on CD-ROM. These estimates were computed by Dr SS Smith, who is solely responsible for the accuracy and appropriateness of the calculations.
¶Estimates were based on two stage DEALE transformations[14] to estimate yearly relapse transition probabilities for short-term (1–2 year) and long-term quitters based on National Health and Nutrition Examination Survey data.
**No data were available for this age group, so we used a conservative assumption that the mortality was not increased in current smokers relative to former for those less than 30 years old.
††Estimates were derived from the Cancer Prevention Study II (CPS-II), using the above sources, as well as unpublished CPS-II data provided by MJ Thun (personal communication). Data are stratified by age and sex, but are independent of duration of abstinence for former smokers.

both the OTC and ℞ scenarios included: (a) the total number of smokers who quit at six months; (b) overall smoking-attributable mortality; and (c) life expectancy of an average smoker using state-transition (Markov) modelling.

DATA SOURCES
Modelling required estimates derived from diverse sources. A MEDLINE literature search was conducted for relevant literature on model parameters. Whenever possible, effectiveness data was preferentially chosen over efficacy data. Population estimates were based on 1990 census data.[16] In addition, several national sur-

veys were used to provide population-based estimates, including the 1990 and 1992 National Health Interview Surveys,[17 18] (NHIS) to provide estimates of smoking prevalence and smoking cessation attempts, and the National Health and Nutrition Examination Survey–I (NHANES–I) and the NHANES Epidemiologic Followup Survey[2] to provide the probability of smoking relapse.

Estimates of the rate of use of nicotine replacement in the OTC scenario were based on marketing surveillance of nicotine replacement therapy use, performed by Shiffman and colleagues.[14] These investigators determined the ratio of use of nicotine products for non-prescription availability compared with prescription availability. We used this ratio multiplied by our estimates for prescription use of nicotine replacement therapy to calculate the rates of use in the over-the-counter setting.

Smoking cessation rates for NRT quitters under both scenarios were derived from a prospective trial of simulated non-prescription nicotine patch use.[19] As noted, we use nicotine patch data as a proxy for nicotine replacement therapy in general, due to the availability of the data on over-the-counter use for this form of replacement. A prospective cohort study was conducted using 2367 participants recruited from public locations such as shopping malls; participants purchased patches at estimated retail price, and were followed up to determine quit rates. Participants lost to follow up in this study were considered to have relapsed. We assume for this analysis that the six-month quit rates for smokers using nicotine replacement was equivalent in the OTC and ℞ scenarios. Post-marketing surveillance using retrospective cohort data on prescription nicotine patch use[19] suggests that the six-month quit rate may actually be lower in the prescription setting. Thus, this assumption is a conservative one which will bias the analysis in favour of the prescription scenario by underestimating the over-the-counter public health benefit. We examine changes in this assumption in sensitivity analysis.

Whenever possible, age-specific and sex-specific data were used in the model. All quit rates are based upon self-reported continuous quit rates which were the most consistently available data. Table 1 provides a summary of parameters used for the baseline case for the model. (Parameter estimates stratified by age and sex from these studies are available in a technical report available on request from the authors.)

THE DECISION MODEL
A decision tree was constructed (figure 1) to estimate the number of current smokers who would quit long-term (six months) in the OTC and ℞ scenarios for each age and sex stratum. In both scenarios, a smoker has a chance of making a quit attempt using nicotine replacement therapy, a chance of making a quit attempt without nicotine replacement, and a chance of not making a quit attempt. We assume for the baseline analysis that the total
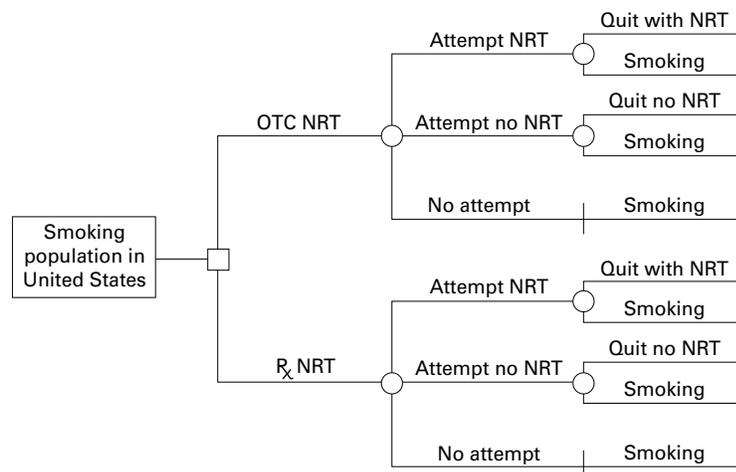

Figure 1 Decision tree for determining the public health benefits of the two scenarios of availability of nicotine replacement therapy. Public health benefits shown in the tree include the number of quit attempts and the number of long-term (six-month) quits. NRT = nicotine replacement therapy, OTC = over the counter, ℞ = prescription.

Table 2   Baseline results

	R̸ Scenario*	OTC Scenario†
Number of adult smokers in the United States	47 002 476	47 002 476
Number willing to try NRT per year	1 014 630	2 556 867
Willing to try NRT per year (%)	2.2	5.4
Quit rate of smokers using NRT at six months (%)	10.8	10.8
Number of quits using NRT at six months	109 685	276 405
Gain in number of quits for OTC scenario at six months	NA	91 151
Total number of quits at six months	420 330	511 480
Life expectancy of average smoker (years)	34.211	34.407
Gain in life expectancy for average smoker (years)	NA	0.196
Smoking-attributable mortality rate (based on six-month data) (deaths per year)	412 617	412 269
Reduction in smoking-attributable mortality rate (based on six-month data) (deaths per year)	NA	348 (0.1%)
Reduction in smoking-attributable mortality rate for OTC scenario (based on five-year data) (deaths per year)	NA	2940 (0.7%)

*Nicotine replacement therapy (NRT) available only by prescription.
†Nicotine replacement therapy available over the counter (OTC).
NA = not applicable.

chance of making a quit attempt by any method is the same for both scenarios. We also assume that any patterns in changes of use of other smoking cessation methods, such as behavioural counseling, would not significantly affect cessation rates for smokers quitting without nicotine replacement in either scenario of nicotine replacement availability. Both of these assumptions were examined in sensitivity analysis.

Markov state-transition models[20] were created to estimate the life expectancy of an average person in each stratum. Each model consisted of five states, representing: current smokers; those quitting for a year or less; those who have quit for one to two years; long-term quitters; and those who have died. These state transition models represent each smoker in the simulation as being in one of the five mutually exclusive states for any particular one-year period. Probabilities were calculated for a person in one state (for example, long-term quitter) to transition to any other state (such as smoking) in the following year. The three quit states allow representation of a lower relapse rate for longer term quitters (more than two years) compared with more recent quitters.[2] Mortality for current and former smokers was

stratified by age and sex,[1 18 21] however, data were not available to calculate this parameter for duration of cessation, so rates are independent of duration of abstinence for former smokers.

For each age and sex stratum, the initial distribution of cohort members across the states was determined by the outcome of the decision tree for that stratum. The model calculated life expectancy until the surviving members of the cohort reached age 100. Transition probabilities for the Markov models were age and sex dependent.

Results

BASELINE RESULTS

Major outcomes of the analysis are shown in table 2. Key findings are that making nicotine therapy available over the counter would result in approximately 1.1 million additional smokers attempting to quit using nicotine replacement therapy in the first six months, and an estimated 91 151 additional smokers would have quit at the end of six months. The number of additional quitters from the current cohort of smokers would continue to increase over time to a maximum of 1.7 million additional quitters at 25 years in the OTC scenario compared with the R̸ scenario (figure 2).

Reclassifying nicotine therapy as non-prescription would also have a positive impact on life expectancy. Across the total cohort of more than 47 million smokers (including continuing smokers and eventual quitters), the average smoker could be expected to live 0.20 years (2.4 months) longer in the over-the-counter scenario than in the prescription scenario (table 2). The impact of permanently quitting smokers on gain in life expectancy on *successful quitters* is presented in table 3. On average, each of these new quitters will gain an average of 4.4 years of life compared with smokers who never quit. Thus, the average gain in life expectancy represents a large life expectancy gain that accrues to the small percentage of smokers who would quit in the non-prescription availability setting but not in the prescription setting.

Based on the proportion of quitters at six months in the OTC scenario compared with that in the R̸ scenario, we estimated a reduction in the all-cause, smoking-attributable mortality rate of 348 deaths per year. At five years, our model predicts a decrease in the all-cause, smoking-attributable mortality rate of 2940 deaths per year for the over-the-counter scenario, due to the increased
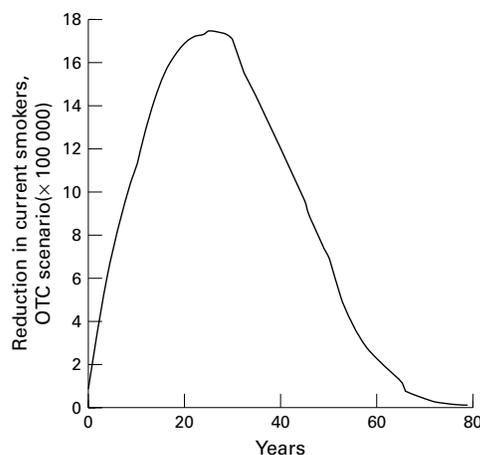
Figure 2   Reduction in the number of smokers in the over-the-counter (OTC) scenario compared with the prescription (R̸) scenario, over time. The reduction is based on the difference in current smokers between the two scenarios, adjusted to the population size of the OTC scenario, for the original cohort of 47 million adult smokers.

Table 3   Gain in life expectancy for smokers who successfully quit smoking*

Age	Men	Women	Total
18–24	6.30	4.01	5.28
25–44	5.85	3.78	4.92
45–64	4.26	3.43	3.86
≥65	1.91	1.33	1.59
Total	5.22	3.47	4.41

*Gain in life expectancy (years) for individual smokers who successfully and permanently quit smoking today, compared with smokers who continue to smoke for the rest of their lives. Totals represent average life expectancy weighted by the number of people in each age and sex stratum.

Table 4 Sensitivity analyses

Parameter*	Gain in number of quits at six months (OTC scenario)	Gain in life expectancy† (OTC scenario)
Baseline	91 151	0.196
Change in probability of attempting to quit by any method (baseline average = 0.31)‡		
0.75 *baseline (average = 0.23)	68 363	0.163
1.25 *baseline (average = 0.39)	113 939	0.222
Two quit attempts per year for those attempting to quit by any method (baseline = 1 per year)	180 661	0.266
Relative chance of quit attempt by any method, OTC to ℞ (baseline 1 to 1):		
0.9 to 1	40 003	0.108
1.1 to 1	142 299	0.280
1.3 to 1	244 595	0.437
Threshold value§: 0.79 to 1		
Probability of using NRT should a quit attempt be made (both scenarios; baseline average = 0.14 ℞, 0.36 OTC)‡		
0.5 *baseline (average = 0.07 ℞, 0.18 OTC)	45 576	0.104
0.75 *baseline (average = 0.11 ℞, 0.27 OTC)	68 363	0.152
1.25 *baseline (average = 0.18 ℞, 0.45 OTC)	113 939	0.238
Threshold value§: 0		
Relative chance of using NRT for those quitting in OTC scenario compared with chance of using NPT in ℞ scenario (baseline average = 2.52 to 1)‡		
0.5 *baseline (average = 1.26 to 1)	15 592	0.035
0.8 *baseline (average = 2.02 to 1)	60 927	0.133
1.2 *baseline (average = 3.02 to 1)	121 375	0.257
Threshold value§: 0.40; *baseline (average = 1 to 1)		
Probability of a successful quit at six months for those attempting with NRT in the ℞ scenario (OTC scenario probabilities held constant; baseline average = 0.106)‡		
1.25 *baseline (average = 133)	63 730	0.137
1.5 *baseline (average = 0.159)	36 309	0.080
2.0 *baseline (average = 0.212)	(18 534)	(0.029)
Threshold value§: 1.86; *baseline (average = 0.197)		
Probability of a successful quit at six months for those attempting with NRT in the OTC scenario (℞ scenario probabilities held constant; baseline average = 0.106)‡		
0.5 *baseline (average = 0.053)	(47 052)	(0.096)
0.75 *baseline (average = 0.080)	22 050	0.055
1.25 *baseline (average = 0.133)	160 252	0.326
Threshold value§: 0.66 *baseline (average = 0.070)		
Probability of a successful quit at six months for those attempting with NRT (baseline average 0.106 ℞, 0.106 OTC)‡		
1.2 *baseline in ℞ scenario (average = 0.127) and, 0.8 *baseline in OTC scenario (average = 0.084)	13 933	0.037
Probability of a successful quit at six months for those attempting without NRT (baseline average = 0.049)‡		
0.8 *baseline (average = 0.039)	106 265	0.235
1.2 *baseline (average = 0.059)	76 037	0.160
2.0 *baseline (average = 0.098)	15 581	0.040
Threshold value§: 2.3; *baseline (average = 0.113)		
Probability of a successful quit at six months for fraction of those attempting without NRT but with non-pharmacological therapy in OTC scenario (baseline average = 0.049)‡		
0.75 *baseline (average = 0.037)	32 382	0.115
0 *baseline (average = 0)	(143 924)	(0.150)
Threshold value§: 0.41 *baseline (average = 0.020)		

NRT = nicotine replacement therapy; OTC = over the counter, ℞ = prescription.
*Changes in parameters noted as a multiplier; *baseline represents the values of the parameter across age and sex strata multiplied by the number to achieve the result listed.
†Measured in average years of life gained for an individual smoker.
‡The weighted average is the average of the values across age and sex strata adjusted to the American adult smoking population. These numbers are provided for reader reference; the analyses were performed using adjustment of each of the strata by the multiplier listed.
§The threshold value is the value of the parameter at which the life expectancy is equal in both the ℞ and the OTC scenarios.

number of quitters in this scenario compared with the prescription scenario (table 2). For the original cohort of 47 million smokers, this gap between the smoking attributable mortality in the non-prescription setting and the prescription setting would continue to widen for approximately 30 years.

SENSITIVITY ANALYSES

Results of the sensitivity analyses demonstrated that the model results were robust for a wide range of changes in the baseline parameters (table 4). The results were most sensitive to changes in the parameter values of the relative chance of making a quit attempt by any method, and the relative probabilities of a successful quit at six months for the OTC and ℞ scenarios. If, for example, the smokers are 10% more likely to attempt to quit by any method in the OTC scenario compared with the ℞ scenario, then the gain in number of quits at six months for the OTC scenario increases by 56% over baseline, and the gain in life expectancy for the OTC scenario increases

by 43%. Conversely, if either the chance of a successful quit at six months is either twice what we predict for the ℞ scenario, or a half of what we predict for the OTC scenario, then the ℞ scenario has more quitters and a better life expectancy.

Threshold values from the sensitivity analyses are also shown in table 4. Threshold values are the values of the model parameters at which there is no longer a life expectancy benefit for smokers in the non-prescription scenario compared with the prescription scenario. For example, if smokers were only 79% as likely (or less) to attempt to quit by any method in the OTC scenario compared with the ℞ scenario, then the OTC scenario would not have a life expectancy advantage.

Discussion

Smoking is a major source of morbidity and mortality in the United States. Thus, policies that even modestly improve smoking cessation rates have the potential to yield large public health benefits. In this analysis, we show that

making nicotine replacement therapy using transdermal patches and nicotine gum available over the counter rather than prescription-only would result in a large increase in the number of successful quitters each year, a reduction in smoking-attributable mortality, and an increase in the life expectancy of smokers. The gain in life expectancy for an average smoker in the over-the-counter setting is 0.196 years; in comparison, the gain in screening 40-year-old men and 40-year-old women for hypertension would be an increase in life expectancy of 0.03 years and 0.01 years, respectively.[22]

Sensitivity analyses demonstrate that the over-the-counter use has a relative benefit compared with prescription use under a wide variety of assumptions. Perhaps the area of greatest uncertainty within the analysis is the six-month effectiveness data for both prescription and non-prescription nicotine replacement therapy. Data are available on NRT-assisted quit rates[5]; these represent primarily *efficacy* results of clinical trials. In contrast, the analyses in this model used data estimating *effectiveness* of nicotine replacement under the OTC scenario. Surveillance data suggest that effectiveness of prescription-only patch use may have a 40% lower six-month success rate than we use for the baseline model.[19] Potential quitters willing to use NRT as an over-the-counter medication may, on average, have fewer or less severe factors for relapse.[23] In contrast, smokers who seek cessation services (including NRT) through health-care providers may, on average, include people with a greater number or level of relapse risk factors.[10] If the six-month cessation rate for prescription use nicotine therapy is lower than we have estimated, then the actual benefits would be greater than we have calculated. Even if the six-month cessation rates for non-prescription nicotine replacement therapy use are 20% worse than we have estimated, and that of the prescription nicotine replacement use 20% better than estimated, our model still predicts a small benefit for the non-prescription availability setting.

There are several caveats that should be considered when evaluating our results. First, there are no randomised clinical trial data linking NRT-based smoking cessation programmes to overall reduction in mortality. Next, we do not explicitly address the issue of adverse effects of nicotine replacement. Since the analysis only addresses mortality associated with smoking, we did not include adverse effects because death directly attributable to NRT therapy itself is an exceedingly rare event, and thus would not change the results of the analysis. Other adverse effects of nicotine replacement therapy—for example, skin irritation from the transdermal patch—tend to be transitory and produce little impact on overall health. Finally, we do not address the economic impact of making nicotine replacement available without prescription.

Overall, we have found that making nicotine replacement therapy available without prescription would result in substantial public health benefit. By implementing a policy to make nicotine patches and gum available as over-the-counter medications for smoking cessation, the number of current smokers would significantly decrease over time, and smoking-attributable mortality would decline as well.

1 US Department of Health and Human Services. *Reducing the health consequences of smoking: 25 years of progress. A report of the Surgeon General, 1989.* Rockville, Maryland: Public Health Service, Centers for Disease Control, Office on Smoking and Health, 1989. (DHHS Publication No (CDC) 89-8411.)
2 US Department of Health and Human Services. *The health benefits of smoking cessation. A report of the Surgeon General, 1990.* Rockville, Maryland: Public Health Service, Centers for Disease Control, Office on Smoking and Health, 1990. (DHHS Publication No (CDC) 90-8416.)
3 Gallup G Jr, Newport F. Many Americans favor restrictions on smoking in public places. *Gallup Poll Monthly* 1990;**298**:19.
4 Cohen S, Lichtenstein E, Prochaska JO, *et al.* Debunking myths about self-quitting: evidence from 10 prospective studies of persons who attempt to quit smoking by themselves. *Am Psychol* 1989;**44**:1355–65.
5 Fiore MC, Smith SS, Jorenby DE, *et al.* The effectiveness of the nicotine patch for smoking cessation: a meta-analysis. *JAMA* 1994;**271**:1940–7.
6 Silagy C, Mant D, Fowler G, *et al.* Meta-analysis on efficacy of nicotine replacement therapies in smoking cessation. *Lancet* 1994;**343**:139–42.
7 Orleans CT, Resch N, Noll E, *et al.* Use of transdermal nicotine in a state-level prescription plan for the elderly—a first look at "real-world" patch users. *JAMA* 1994;**271**:601–7.
8 Pierce JP, Gilpin E, Farkas AJ. Nicotine patch use in the general population: results from the 1993 California Tobacco Survey. *J Natl Cancer Inst* 1995;**87**:87–93.
9 Fiore MC, Novotny TE, Pierce JP, *et al.* Methods used to quit smoking in the United States—do cessation programs help? *JAMA* 1990;**263**:2760–5.
10 Lichtenstein E, Hollis J. Patient referral to a smoking cessation program: who follows through? *J Fam Pract* 1992;**34**:739–45.
11 Marion Merrell Dow, Inc. *Nicoderm (Nicotine transdermal system) prescribing information.* Kansas City, Missouri: Marion Merrell Dow, 1991.
12 Fiore MC, Jorenby DE, Baker TB, *et al.* Tobacco dependence and the nicotine patch: clinical guidelines for effective use. *JAMA* 1992;**268**:2687–94.
13 Benowitz NL. Nicotine replacement therapy: what has been accomplished—can we do better? *Drugs* 1993;**45**:157–70.
14 Shiffman S, Gitchell J, Pinney JM, *et al.* Public health benefit of over-the-counter nicotine medications. *Tobacco Control* 1997;**6**:306–10.
15 Sox HC, Blatt MA, Higgins MC, *et al. Medical decision making.* Boston, Massachusetts: Butterworths, 1988.
16 US Department of Commerce. *Statistical abstract of the United States 1994,* 114th ed. Washington, DC: Department of Commerce, 1994.
17 US Centers for Disease Control. Cigarette smoking among adults—United States, 1990. *MMWR* 1992;**41**:354–5, 361–2.
18 US Centers for Disease Control. Cigarette smoking-attributable mortality and years of potential life lost—United States, 1990. *MMWR* 1993;**42**:645–9.
19 SmithKline Beecham, Marion Merrell Dow. *Supplement to FDA application 20–165 for approval of Nicoderm 21 mg/day, 14 mg/day, 7 mg/day.* Pittsburgh, Pennsylvania: SmithKline Beecham; Kansas City, Missouri: Marion Merrell Dow.
20 Beck JR, Pauker SG. The Markov process in medical prognosis. *Med Decision Making* 1983;**3**:420–58.
21 Thun MJ, Day-Lally C, Myers DG, *et al.* Trends in tobacco smoking and mortality from cigarette use in Cancer Prevention Studies I (1959–1965) and II (1982–1988). In: *Changes in cigarette-related disease risks and their implications for prevention and control.* Bethesda, Maryland: National Cancer Institute, 1997: chapter 4. (NCI Monograph No 8.)
22 Littenberg B, Garber AM, Sox HC. Screening for hypertension. *Ann Intern Med* 1990;**112**:192–202.
23 Killen JD, Fortmann SP, Kraemer HC, *et al.* Who will relapse? Symptoms of nicotine dependence predict long-term relapse after smoking cessation. *J Consult Clin Psychol* 1992;**60**:797–801. Hughes JR, Gulliver SB, Fenwick JW, *et al.* Smoking cessation among self-quitters. *Health Psychol* 1992;**11**:331–4.
24 Hughes JR, *et al.* Smoking cessation among self-quitters. *Health Psychol* 1992;**11**:331–4.