

Impact of Over-the-Counter Sales on Effectiveness of Pharmaceutical Aids for Smoking Cessation

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OVER ONE THIRD OF US smokers attempt cessation each year¹⁻⁵; however, the success rate per attempt is low.^{2,6,7} Few smokers seek assistance for cessation,^{3,8,9} and those who do tend to be more dependent.^{3,9,10} During the 1990s, following clinical trials indicating efficacy, a variety of pharmaceutical cessation aids became available.¹¹⁻¹⁹ Designed to lessen nicotine withdrawal symptoms (eg, anxiety, irritability, intense craving), these aids were recommended as adjuvants to behavioral therapies.¹¹⁻¹⁴ In the controlled-trial setting, with well-monitored protocols, nicotine replacement therapy (NRT) and the antidepressant bupropion increased success for moderate to heavy smokers (≥ 15 cigarettes/d) by 50% to 100%.¹¹⁻¹⁸ There is no consensus of a benefit for light smokers (< 15 cigarettes/d).

In the early 1990s, we reported a possible population cessation advantage for NRT, when prescribed and used together with counseling or self-help materials.¹⁰ Since then, the nicotine patch became available over-the-counter in 1996, and the efficacy of bupropion was demonstrated in clinical trials.^{15,17,18} Pharmaceutical companies have marketed these products extensively, both to physicians and the public.¹⁹ A pack-a-day cigarette habit costs about \$150 for 6 weeks in California, nearly iden-

Context Successful smoking cessation is a major public health goal. In controlled clinical trials, nicotine replacement therapy (NRT) and the antidepressant bupropion have been shown to significantly increase cessation rates only for moderate to heavy smokers (≥ 15 cigarettes/d). Nicotine replacement therapy is heavily promoted to the general population by both the pharmaceutical industry and tobacco control advocates.

Objective To examine trends in smoking cessation, pharmaceutical cessation aid use, and success in cessation in the general California population.

Design, Setting, and Participants The large population-based California Tobacco Surveys of 1992, 1996, and 1999, including 5247 (71.3% response rate), 9725 (72.9% response rate), and 6412 (68.4% response rate) respondents, respectively.

Main Outcome Measures Rates of cessation attempts (≥ 1 day) among smokers in the last year, use of pharmaceutical aids (mostly over-the-counter products since 1996), and cessation success.

Results Between 1992 and 1999, cessation attempts among California smokers increased 61.4% (from 38.1% to 61.5%), and NRT use among quitters increased 50.5% (from 9.3% to 14.0%). A total of 17.2% of quitters used NRT, an antidepressant, or both as an aid to cessation in 1999. In 1996 and 1999, the median duration of aid use (14 days) was much less than recommended, and only about 20% of users had adjuvant one-on-one or group behavioral counseling. Use of NRT increased short-term cessation success in moderate to heavy smokers in each survey year. However, a long-term cessation advantage was only observed before NRT became widely available over-the-counter (August 1996). In 1999, no advantage for pharmaceutical aid users was observed in either the short or long term for the nearly 60% of California smokers classified as light smokers (< 15 cigarettes/d).

Conclusion Since becoming available over the counter, NRT appears no longer effective in increasing long-term successful cessation in California smokers.

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tical to the cost of the nicotine patch but about half the cost of nicotine gum, if used as recommended. In some instances (eg, California's Medi-Cal program), pharmaceutical cessation aids are supported as a prescription benefit, reducing the cost disincentive for use.^{12,20-22}

We report population trends and effectiveness in NRT use by recent smokers undergoing cessation in Cali-

fornia from 1992 to 1999. In 1999, we examined duration of aid use, if aid users would recommend these products to other smokers, whether assis-

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tance in paying for the medication was associated with longer use, and the use of adjuvant behavioral assistance. Finally, we searched for evidence that, collectively, pharmaceutical aids increased successful cessation among moderate to heavy and light smokers.

METHODS

Data Sources

The analyses for the present study focused on smokers in the previous year from the 1992 (n=5247), 1996 (n=9725), and 1999 (n=6412) California Tobacco Surveys (CTS). The methodology for the CTS (large population surveys undertaken since 1990) is described elsewhere.²³⁻²⁵ Briefly, a random-digit-dialed telephone protocol enumerates household residents, gathering demographic information and smoking status. An adult sample was scheduled for interview on tobacco-related issues, with selection probability related to smoking status. Completed interviews were obtained for 71.3% of adults in 1992, 72.9% in 1996, and 68.4% in 1999. In all years, there were slight differences in demographics between those selected and those who completed interviews. Following standard practices, the CTS are weighted to make the data representative of the California population in a 2-step procedure: for the probability of respondent selection and for nonresponse, using ratio adjustment to census data.²³⁻²⁵ Duplicate estimates of California smoking prevalence from the US Bureau of the Census in 1993, 1996, and 1999 are within 1 percentage point.²⁶

Survey Items Analyzed

Survey questions were drawn, wherever possible, from previous national surveys. Respondents were asked about current smoking status, whether they smoked a year previously and how much, whether they had in the past year quit intentionally for a day or longer, which is the standard definition of a meaningful cessation attempt,²⁷ how long they were off cigarettes the last time they attempted cessation, and if they used a pharmaceuti-

cal aid or had other assistance for their most recent attempt in the last year. If so, they were asked how long they used the aid, whether they would recommend it to a friend, and who paid for it. Following a validation study, only the most recent cessation attempt was assessed.²⁸ A smoker in the last year either smoked currently or a year previously. Cessation duration for recent former smokers (12 months ago but not currently) was the difference between the survey date and when they last smoked regularly. Average daily consumption a year ago was computed by multiplying the number of days smoked by the number of cigarettes smoked on those days and dividing the product by 30 days.

Statistics

These population surveys were not exclusively designed to measure cessation aid use by smokers; however, sample sizes were large enough to address effectiveness of NRT use. All estimates were computed using sample weights²³⁻²⁵ and are presented together with 95% confidence intervals (CIs). Variance estimation and statistical inference for these complex surveys used a jackknife procedure²⁹ from the statistical package *WesVarPC* version 2.0 (Westat Inc, Rockville, Md).³⁰

Because this is not a randomized study, individuals who choose to use a pharmaceutical aid likely differ from nonusers. In addition to stratifying for daily cigarette consumption (<15 or ≥15 cigarettes/d), we used Cox proportional hazards regression analyses to examine the effect of pharmaceutical aid use on duration of abstinence of the most recent cessation attempt in the last year, adjusting for demographics (age, sex, race/ethnicity, educational level) and reported cigarette consumption a year earlier. The Cox proportional hazards regression model considers both those who relapsed from cessation and those who quit at the time of the survey. Since it is unknown how long those who were still in cessation when interviewed will

remain abstinent, their contribution to the analysis is censored to the duration observed. A specially-written SAS version 6 program (SAS Institute, Cary, NC) derived the appropriate jackknifed variance estimates for the regression coefficients to determine whether any was significantly different from zero. We verified the proportional hazards assumption for each predictor with the Grambsch and Therneau³¹ procedure, available in the statistical package *S-plus* version 2000 (MathSoft Inc, Cambridge, Mass).

RESULTS

Trends in Assistance Over Time

The weighted percentages (95% CI) of California smokers in the last year with a cessation attempt lasting a day or longer were 38.1% (36.1%-40.1%) in 1992, 56.0% (55.0%-57.0%) in 1996, and 61.5% (60.0%-63.0%) in 1999, an increase of 61.4% in the 7-year period.

For smokers' most recent cessation attempts, overall assistance use (self-help, counseling, NRT, or in 1999, an antidepressant) increased from 18.4% (16.0%-20.8%) in 1992 to 19.3% (18.0%-20.6%) in 1996 and to 22.1% (20.3%-23.9%) in 1999; the increase from 1996 to 1999 was statistically significant ($P=.01$). Group counseling for the most recent attempt was received by 2.9% (2.1%-3.7%) of those who made a cessation attempt in 1992, 2.1% (1.6%-2.6%) in 1996, and 2.3% (1.7%-2.9%) in 1999. One-on-one counseling was received by 2.8% (1.6%-4.0%) of those who made a cessation attempt in 1992, 3.4% (2.7%-4.1%) in 1996, and 2.8% (2.2%-3.4%) in 1999. Self-help materials were used by 7.9% (6.2%-9.6%) of those who made a cessation attempt in 1992, 10.1% (8.6%-11.6%) in 1996, and 11.2% (9.8%-12.6%) in 1999.

Nicotine replacement therapy use for the most recent cessation attempt increased significantly from 9.3% (7.5%-11.1%) in 1992 to 12.7% (11.6%-13.8%) in 1996, and to 14.0% (12.7%-15.3%) in 1999, an increase of 50.5% from 1992 to 1999 ($P<.001$). In 1999,

the percentage of individuals using any pharmaceutical aid was 17.2% (15.7%-18.7%). Because we assessed only the most recent cessation attempt, our estimates of the annual number of NRT users are conservative. In California, an estimated 116 209 smokers used NRT in 1992, 337 142 in 1996, and 423 290 in 1999, representing a 3.6-fold growth in NRT use.

Smokers could use multiple pharmaceutical-aid products. In 1999, 5.4% (4.5%-6.3%) used nicotine gum, 10.7% (9.5%-11.9%) used a nicotine patch, no respondent reported using a nicotine in-

halant, and 5.2% (4.3%-6.1%) used an antidepressant (bupropion, 3.2% [2.6%-3.8%]). Of NRT users, 14.6% (11.6%-17.6%) also used an antidepressant.

Cigarette Consumption and Pharmaceutical Aid Use in 1999

Because of small sample sizes for specific aids, FIGURE 1 shows the percentage of quitters using any pharmaceutical aid in each survey year, according to cigarette consumption a year previously. In all years, aid use was low among those who made a cessation at-

tempt who smoked less than 5 cigarettes/d and increased markedly in each higher consumption category. Between 1996 and 1999, aid use increased significantly in groups consuming 5 to 9 cigarettes/d ($P=.048$), 10 to 14 cigarettes/d ($P=.01$), and 20 to 24 cigarettes/d ($P<.001$). Of the additional 161 865 smokers using a pharmaceutical aid in 1999 compared with 1996, 59 273 (37%) were from the lighter smoking group for whom pharmaceutical aids are not currently recommended.

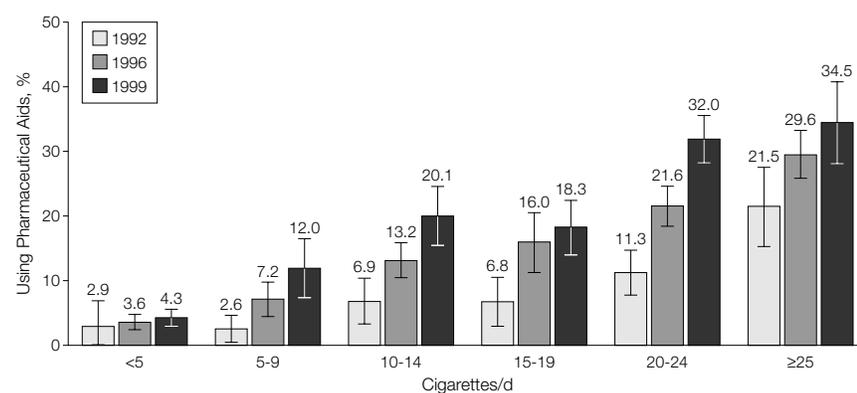
Characteristics of Pharmaceutical Aid Use in 1999

Most smokers paid for NRT themselves, but some smokers' insurance plans covered physician-prescribed antidepressants (TABLE). The vast majority of NRT users say they would recommend it to a friend, but antidepressant users were less enthusiastic. Individuals who were still in cessation when interviewed had a more favorable opinion than relapsers.

Mean duration of NRT use in 1999 (28.2 days; 95% CI, 25.2-31.2) was not statistically different from the 29.7 (21.8-37.6) days in 1992 or the 26.2 (22.5-29.9) days in 1996. Use duration was skewed and ranged widely; median use was only 14 days. Of NRT users who remained abstinent after stopping aid use, 12.5% (6.7%-18.3%) used the product more than 12 weeks. Nearly one third (31.7% [27.4%-36.0%]) of NRT users relapsed and quit aid use simultaneously. Approximately a quarter (23.3% [19.1%-27.5%]) continued NRT use after relapse (median, 21 days; interquartile range, 7-42 days).

Duration of NRT use was related to payment mode ($P=.02$). Of smokers whose insurance completely covered NRT, 39.5% (22.1%-56.9%) used it 6 weeks or longer. Of smokers who shared the expense, 44.3% (22.4%-66.2%) used it 6 weeks or longer, but for smokers who paid the entire cost, only 21.8% (17.3%-26.3%) used NRT 6 weeks or longer. Nicotine replacement therapy users reported more be-

Figure 1. Use of Pharmaceutical Aids for Most Recent Cessation in 1992, 1996, and 1999 According to Self-reported Cigarette Consumption a Year Before Interview



Data are shown as weighted percentages and 95% confidence intervals.

Table. Details of Users of Cessation Aids in 1999

	Weighted Percentage (95% Confidence Interval)	
	Nicotine Replacement	Antidepressants
Who paid for aid		
Smoker completely	56.5 (52.3-60.7)	35.3 (27.9-42.7)
Insurance completely	4.7 (2.8-6.6)	24.1 (16.7-31.5)
Both partially	5.5 (3.5-7.5)	31.7 (22.5-40.9)
Other/unknown	33.3 (28.3-38.3)	8.9 (4.1-13.7)
Would recommend aid to friend		
Overall	87.7 (84.3-91.1)	60.1 (53.5-66.7)
Former	96.0 (93.2-98.8)	65.4 (48.2-82.6)
Current (relapsed)	79.3 (75.2-83.4)	58.3 (50.7-65.9)
Duration of use, days		
Mean	28.2 (25.2-31.2)	25.0 (20.5-29.5)
Median (interquartile range)	14.0 (7.0-30.0)	14.0 (7.0-30.0)
Still quit after stopped aid	44.9 (40.3-49.5)	62.8 (54.8-70.8)
Use behavioral assistance		
Any	51.3 (47.2-55.4)	34.8 (27.3-42.3)
Group counseling	9.3 (6.8-11.8)	7.8 (4.6-11.0)
One-on-one counseling	7.5 (5.2-9.8)	13.0 (8.0-18.0)
Self-help materials	48.3 (44.0-52.6)	31.6 (24.5-38.7)

havioral assistance than antidepressant users, but both groups relied mostly on self-help materials.

Quitting Success

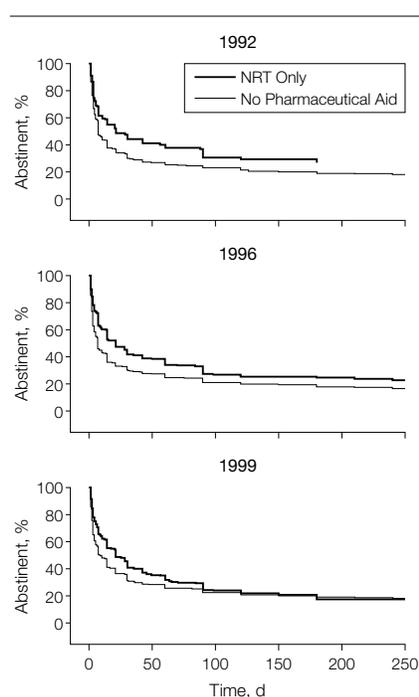
Cox proportional hazards regression analyses of cessation duration for moderate to heavy smokers, adjusted for demographics and smoking level a year previously, indicated a significant effect for NRT use (FIGURE 2) and smoking level for each year ($P < .001$ and $P = .008$ in 1992; $P < .001$ and $P = .02$ in 1996; and $P = .002$ and $P = .01$ in 1999, respectively). However, in contrast with 1992 and 1996, the effect in 1999 was only short-term; after about 3 months, the curves are nearly identical. In all years, the curves for those not using any pharmaceutical aids were nearly identical over the entire range of cessation duration, and the curve for 1996 NRT users is between the curves for 1992 and 1999 NRT users.

FIGURE 3 shows that in 1999, when users of any aid are compared with nonusers, the short-term advantage is present for the moderate to heavy smokers but not for light smokers. While aid use and level of consumption were statistically significant ($P < .001$ and $P = .01$, respectively) in the Cox proportional hazards regression analysis for the moderate to heavy smokers, neither variable was significant in the light smokers.

COMMENT

Despite widespread promotion of pharmaceutical aids for cessation throughout the 1990s, and an 85% increase in the percentage of quitters using any such aid from 1992 to 1999, the percentage of California quitters using a pharmaceutical aid in 1999 for their most recent cessation attempt was low (17.2%). Nonetheless, the large increase in smokers making cessation attempts boosted the pharmaceutical aid market more than 3-fold from 1992 to 1999. This increase occurred as the percentage of the California smokers who are moderate to heavy daily smokers decreased from 56.4% (54.7%-58.1%) in 1990 to 40.6% (38.9%-42.3%) in 1999,²⁵ and reflected

Figure 2. Relapse to Smoking in Moderate to Heavy Smokers by Use of Nicotine Replacement Therapy in 1992, 1996, and 1999

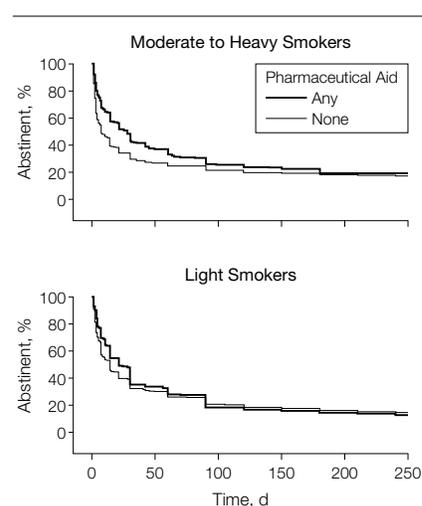


NRT indicates nicotine replacement therapy. Moderate to heavy smokers is defined as 15 cigarettes/d or more. Relapse times were adjusted in a Cox proportional hazards regression analysis for demographics and cigarette consumption level a year earlier.

the successful recruitment of light smokers, for whom evidence of a potential benefit is lacking.

In 1999, although collectively pharmaceutical aids helped moderate to heavy smokers discontinue using cigarettes longer, they were not associated with a clinically meaningful long-term improvement in successful cessation, and no benefit was observed for light smokers. In 1992, NRT was prescribed by physicians only, and physicians or pharmacists may have provided counseling about product use. By mid-August 1996, NRT was widely available over-the-counter.³² Thus, individuals who made a cessation attempt, from the 1996 CTS conducted in September through December who report on cessation attempts any time during the previous year, may or may not have obtained their NRT by pre-

Figure 3. Relapse to Smoking in Moderate to Heavy Smokers and Light Smokers According to Use of Any Pharmaceutical Aid in 1999



Moderate to heavy smokers is defined as 15 cigarettes/d or more and light smokers as less than 15 cigarettes/d. Any pharmaceutical aid indicates nicotine replacement therapy or an antidepressant. Relapse times were adjusted in a Cox proportional hazards regression analysis for demographics and cigarette consumption level a year earlier.

scription. Nonetheless, there appears to be some long-term benefit that was not observed in 1999, when all NRT was obtained over-the-counter.

In 1999, only about half of California aid users managed to discontinue smoking even for a day after they stopped using the aid. There was little evidence that smokers used NRT as a long-term substitute for cigarette smoking. Having insurance co-pay led to longer use, but only about 40% used NRT longer than the recommended minimal period of 6 weeks.^{12,13} However, the loss of long-term effect cannot be completely due to short duration of aid use, as mean duration was similar in all years.

This study adds to concerns that the efficacy of pharmaceutical aids observed in clinical trials may not extend to effectiveness in the general population.^{32,33} There are a number of possible reasons for this mismatch. Trial participants may differ from those who made a cessation attempt in the general population, particularly

with respect to motivation (willingness to tolerate the participant burden involved). Not all trials included in the recent meta-analyses^{12,14-16} used continuous abstinence as the outcome measure. In one study, the preferred measure was abstinence for at least a week at 5 months,¹⁶ which could lead to artificially high cessation rates. Our study analyzed the duration of smokers' most recent intentional cessation attempt in the past year lasting a day or longer (the accepted definition of a serious cessation attempt²⁷), which allows the pattern of relapse to be

examined. Certainly, lack of adherence to recommended guidelines and lack of adjuvant behavioral counseling among California smokers was also a factor. Other studies of over-the-counter patch users documented similar problems,³³⁻³⁶ and some NRT trials that attempted to simulate an over-the-counter setting showed an advantage,³⁷⁻³⁹ but another did not.³³ The present study highlights the need for more research nationwide concerning barriers to more appropriate use of NRT in the nonclinical setting. Finally, the use of bupropion, which

could not be evaluated separately in this study because of small sample size, requires evaluation in the non-clinical setting.

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