

What's New in *Nicotine & Tobacco Research*?

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Does nicotine really do what they say?

Studies consistently find that smokers believe their smoking is mood-enhancing—that it relaxes, increases vigor, reduces anxiety, and heightens pleasure—but does it really? To investigate the direction, size, and consistency of these effects, Kalman and Smith (p.317) conducted a meta-analysis of 21 placebo-controlled studies, 17 in which subjects were administered nicotine nasal spray and 4 in which they received intravenous nicotine. Despite a paucity of adequately powered studies, they were able to conclude that—

- Nicotine increased head rush in a dose-dependent manner in both smokers and never-smokers.
- Nicotine increased vigor for smokers but decreased vigor in never-smokers.
- Nicotine decreased relaxation, although the effects varied according to the route of administration.
- Observed effects were stronger in nonsmokers than in smokers.

The subjective effects of nicotine are likely to differ from the effects of nicotine administered by a nasal spray or intravenous route. However, “the evidence that the subjective effects of nicotine directly mediate its reinforcing effects is quite modest,” the authors note.

NRT, bupropion: Mild effects can pose problems

Recent reports have raised alarm in Europe of possible risks when using bupropion to treat nicotine addiction. What is known about the likely adverse effects of both sustained-release bupropion and nicotine replacement comes mostly from controlled clinical trials, not actual practice. In Spain, Barrueco et al. (p. 335) dealt with both concerns by evaluating the real-world safety of nicotine replacement therapy (NRT), bupropion, and a combination of both treatments. They followed 904 adult smokers in treatment for 3 months. After screening for the most

appropriate therapy, 370 smokers were given NRT, 413 received bupropion, and 121 received combined therapy. Although the adverse effects were mostly mild, many smokers considered them serious enough to discontinue treatment. By the 90th day, 199 had dropped out at least temporarily.

- Adverse effects were found in 43.8% of the smokers at the 15-day check-up, but declined steadily after that to 5.7% at 90 days.
- The effects were more frequent among those on bupropion or combined therapy at 15, 30, and 60 days, but not at 90 days.
- Those on bupropion or combined therapy complained most often of insomnia or sleep problems, even after 90 days.
- After 60 days, adverse effects caused 83 smokers to suspend treatment indefinitely and 116 to interrupt it temporarily.
- Severe or moderate effects more often caused patients receiving bupropion to end treatment either temporarily or indefinitely, but mild effects also caused many to drop out.

“Despite recent scares regarding the use of bupropion SR,” the investigators conclude, “this pharmacological agent is considered safe at the dosages used for treating nicotine addiction, as long as patients are screened for the possibility of seizures and drug interactions before they start treatment, and are monitored regularly.”

A cautionary note: Some of the effects of both NRT and bupropion mimic those of nicotine withdrawal, making it difficult to determine whether they are caused by the treatment itself or its failure to reduce withdrawal symptoms.

Tracking the sources of nicotine intake

It could be argued that a switch to “clean” nicotine by all smokers would result in an immediate reduction in cardiovascular disease and a delayed reduction in respiratory disorders and cancers. That’s because

taking in pure nicotine has not been associated with cancer or respiratory problems and certainly poses a much lower risk for cardiovascular diseases than does ingesting tobacco smoke. However, "It is essential to know the source of consumed nicotine, if a switch from the most contaminated delivery system (smoking) to cleaner systems were to be an active tobacco control strategy," writes Fagerström (p. 343).

In what may be the first effort to estimate the uptake of nicotine from tobacco and nicotine replacement products and to map its consumption in selected countries, the author calculated that daily per-capita consumption of nicotine totaled—

- 8.9 mg in Austria, the nation with the least advanced antismoking climate
- 8.2 mg in Denmark and Sweden
- 8.1 mg in the United States
- 6.1 mg in Norway
- 5.5 mg in Finland

Despite Sweden's second highest per capita consumption of nicotine replacement products (after Iceland), even there the contribution from such products was only 1.3%. As expected, "the dirtiest vehicle (smoked tobacco) in most countries accounts for more than 90% of nicotine intake," Fagerström writes.

Only in Sweden was that not true: There, almost half of all nicotine ingested came from snus, Sweden's version of chewing tobacco, used almost exclusively by men who had been heavy smokers. Swedish men have Europe's lowest rate of smoking-related morbidity, lowest smoking prevalence, and highest intake of nicotine from nonsmoking sources. "Whether these three factors are related and even causally so is currently much debated," Fagerström notes. "It should be of great interest to see how consumption reflects on morbidity or mortality, particularly if the cigarette monopoly on nicotine intake could be broken in countries other than Sweden."

The eight classes of smokers

Most studies classify smokers along a single continuum, such as whether they had ever smoked or still did, whether they were more or less nicotine dependent, their intentions of quitting or not, or their patterns of consumption. Furberg and colleagues (p. 351) sought to refine such classifications to better capture the heterogeneous nature of smoking by analyzing the interview responses of 3,025 individual twins who had smoked regularly at some time in their lives. They examined 18 variables in four domains: demographics, smoking history, nicotine dependence, and quit-attempt history. The analysis revealed eight distinct classes of smokers. Three classes had low nicotine dependence:

- Former smokers who said quitting caused no anxiety or depression. These tended to be well educated and have high extraversion scores.
- Current smokers, only 27% of whom had tried to quit, but with little or no anxiety or depression. These tended to be single and score low on depression and high on extraversion.
- Much like those in the previous class, but with more quit attempts; about half still smoked regularly despite low dependence scores.

Three classes had moderate nicotine dependence:

- Mostly well-educated women (74%) and former smokers (88%) who had tried seriously to quit but experienced high anxiety when they did.
- Mostly married men, all of whom had tried to quit, half without serious depression or anxiety; half of them still smoked.
- Mostly current smokers who had repeatedly tried to quit, but with anxiety and depression. These also had high rates of cocaine abuse or dependence.

Two were highly dependent on nicotine:

- Current smokers, few of whom had ever tried to quit. They also were less educated and had histories of alcohol, cocaine, and marijuana abuse or dependence.
- Current and former (45%) smokers who had started young, were highly dependent on other substances as well, and had tried often to quit, typically with high anxiety or depression. These tended to be married with children, have major depression, and have the highest neuroticism and lowest extraversion scores.

Such groupings could prove valuable, the investigators write. "Acknowledging the complexity of cigarette smoking, and classifying smokers into more specific subgroups ... will enable more accurate evaluation of disease etiology and risk and could lead to more appropriate smoking cessation interventions."

Coping with distractions: Nicotine's role

Studies have shown that nicotine improves performance on vigilance tasks, but little is known about whether that works in the presence of significant distractions. Evidence also suggests that nicotine has a different effect depending on the subject's dopamine type-2 receptor (DRD2) genotype (smoking is more prevalent among those with at least one A1 allele than among those with only A2 pairings), and the type of difficulty encountered.

Gilbert and coauthors (p. 361) tested 56 temporarily abstaining smokers to assess nicotine's effects on their responses to distractions during rapid visual information processing tasks. As single-digit numbers flashed on a computer screen at the rate of 100 per minute, each

subject was asked to depress a key whenever three successive odd or even numbers appeared. Half the time a visual distraction flashed on the screen as well, either at the left, right, or center; in some tests, the distraction was emotional—a positive, negative, or neutral image; in others it was cognitive—an odd or even number they were told to ignore.

- In all tasks, both accuracy and speed increased for those wearing nicotine patches compared to a placebo, but with important variations.
- Nicotine speeded reaction times more when emotional images appeared on the left and when numeric distractions appeared on the right.
- Nicotine tended to improve performance more for those with at least one A1 allele, especially when numeric distractions were displayed on the right.
- Nicotine tended to reduce distraction by negative images more than other types.

Because left-side distractions are processed by the brain's right hemisphere and vice versa, the investigators conclude that their results "suggest that the presence of a DRD2 A1 allele modulates the effects of nicotine attention and distraction in a manner reflecting asymmetries in hemispheric brain function and possibly asymmetries in densities of DRD2 receptors. Our findings also are consistent with the view that nicotine helps individuals filter out distracting or unpleasant stimuli." They note further that nicotine's greatly improved performance against negative images was "consistent with the view that nicotine may reduce negative affect in depressed and anxious individuals by facilitating responses to task-related benign stimuli."

Kids and TV: Watching more, smoking younger

Research demonstrates that movies and television affect smoking rates and attitudes, particularly among the young, but no prior research has studied whether it affects the age at which a youngster starts smoking, an important factor in the consequences of smoking. Gutschoven and Van den Bulck (p. 381) analyzed questionnaire responses of 909 Belgian adolescent smokers and found that they watched television an average of almost 24 hours a week.

Boys, who watched significantly more TV than girls, started smoking earlier in life. If both parents smoked, the adolescent started smoking earlier than if one parent smoked; if neither smoked, the adolescent started later. Not only did those who watched more TV take up smoking earlier, but for each hour they watched per day, the average age at which they started smoking decreased by 2 months. Remarkably, the relationship of the age of taking up smoking and TV viewing was even stronger than that of either gender or parental smoking.

The authors offer three possible explanations: The adolescents are using TV actors who smoke as role models; they are gradually led to adopt the world view of television fiction; or a third, unidentified factor—such as parental supervision or the lack of it—accounts for both TV viewing and smoking history. "Further research," they write, "should examine whether the relationship is causal and whether television acts as a provider of smoking role models or whether it influences smoking attitudes."

Quitters: Who succeeds, who doesn't (the story continues)

Researchers in the early and mid-1990s found that light smokers were more likely to try to quit than heavy smokers, but only those who smoked fewer than five cigarettes a day were more likely to succeed. Times have changed. Levy et al. (p. 387) examined 1998-1999 national survey data from 27,115 adult smokers and quitters to see if that was still true, and to identify factors accounting for who quit successfully and who didn't.

- Heavy smokers were still less likely to try to quit but were more likely to remain abstinent for at least three months when they did.
- Smokers 25 to 44 years old were more likely to try to quit but less likely to succeed than older smokers.
- Women 24 to 44 reported fewer quit attempts than men, but women were generally more likely than men to succeed when they tried.
- Blacks were more likely to try to quit than Whites, but less likely to succeed, and Hispanics were less likely to try but more likely to succeed.
- Smokers with higher education and income were more likely both to try and to succeed at quitting, but that relationship was clearer in relation to education than to income.
- Higher prices motivated smokers to try to quit, and both the price increases and comprehensive antismoking campaigns improved chances of success.

The investigators conclude that "efforts should be directed at older smokers to continue to motivate them to quit, and ... directed at Black, younger, and lighter smokers to improve their success rates."

Swedish way: You snus, you may not lose

Snus, a smokeless tobacco sold in sachets of a gram or less and taken orally, has been credited with lowering smoking rates in Sweden. It is believed that the high pH levels deliver nicotine more efficiently to the bloodstream than U.S. brands of smokeless tobacco because freebase nicotine is rapidly absorbed. But is it really a safe and more effective

nicotine replacement product? Lunell and Lunell (p. 397) compared nicotine delivery by four brands of snus to that of 2-mg nicotine gum by having regular snus users try each product multiple times, once every hour over a day. These were the results:

- The most popular brand, General (1 g) produced plasma concentrations of nicotine similar to those of smoking 25 to 40 cigarettes a day, 2.5 times those of the gum.
- Catch Licorice (1 g) and Catch Mini (0.5 g) produced blood levels similar to moderate smoking of 15 to 20 cigarettes a day, and twice those of the gum.
- Catch Dry Mini (0.3 g) produced blood levels similar to smoking 7 to 10 cigarettes per day, approximating that of the gum.

Because some studies have raised concern that using snus increases cardiovascular risk, the researchers also tested snus for sodium chloride. At the levels found in the four tested brands, it would take about 900 sachets of snus to equal a tablespoon of salt, “suggesting that the risks...due to increased salt load from the use of snus are negligible.”

The disappointing results of nicotine replacement products raise the question of whether the nicotine substitution from these products is too low or too slow. The snus results, the authors write, demonstrate that steady-state nicotine may be sustained at higher levels than available nicotine replacement products achieve. They speculate that “novel [nicotine replacement therapy] products could be targeted at such levels [as snus delivers] to be more effective,” although controlled trials will be needed to determine whether they would actually be more effective.

How to recruit physicians: Make them partners

A physician's advice is effective in getting smokers to quit, but while one survey has shown that physicians identified the smoking status at 70% of adolescent patient visits, they advised the identified young smokers at only 17% of their visits. When the study team set out, as reported by McIntosh and colleagues (p. 405), to test a counseling intervention for adolescents in the offices of community-based pediatricians and family physicians, they expected resistance: Prior research showed that physicians worry that such intervention studies will be too disruptive and time-consuming for their practices. To counter the reluctance, the researchers held focus groups with 30 pediatricians and family practitioners and were told to make physicians full partners. They refined their recruitment strategy based on the focus group advice:

- Practices were sent an introductory letter detailing the study's purposes, benefits, and commitments.

- The study was endorsed by at least one prominent local physician.
- Time, energy, and paperwork commitments were kept to a minimum.
- Physicians received compensation, such as continuing education credits or reimbursement for their time.
- Project trainers provided food and refreshments for all office staff at presentations and training sessions.

The team contacted 185 eligible practices to ask to make a staff presentation during breakfast or lunch hours; 82 declined, citing concerns about disruption and office schedules, but 103 agreed. After the presentations, all but 2 of those 103 made a 1-year commitment to meet the study's need for frequent contacts, maintenance of materials, and completion of three surveys. By the end of a year, 90% were still participating successfully.

At least one key component of the recruitment success, according to the study team, was delaying the final decision to participate until the presentation because that “minimized the chance that the recruiters would be put in the position of appearing to pressure physicians to agree to study enrollment over the phone.” Further research is needed to determine which recruitment components contribute to success and to what degree.

Siblings who smoke: Genes or environment?

When adolescent siblings show the same propensity to smoke, to what extent is that an inherited trait and to what extent does it reflect shared environmental factors, such as the influence of mutual friends or their influence on each other? Answers to such questions have important implications for the progression to regular tobacco use and eventual dependence. Rende and colleagues (p. 413) analyzed smoking frequency data from 2,142 adolescent sibling pairs—both twins and nontwins; both brothers, sisters, and opposite-sex pairs—to determine the degree to which genetic and shared environmental factors influenced high levels of smoking frequency.

They found that the genetic-environment mix was the same for both boys and girls. Both genetic (28% to 35%) and shared environmental factors (25% to 38%) “made notable contributions” to whether adolescents were grouped among the most frequent smokers. This “most striking finding,” the authors report, “should alert researchers to the profound impact of the social environment on frequency of use of cigarettes in adolescence, and particularly to the aspects of the social environment that are common to siblings.... Smoking is, put simply, a familial phenotype....[P]reventive programs that target families...may offer some promise in reducing the

likelihood of initial smoking as well as progression to higher levels of smoking intensity in adolescence.”

Schizophrenia: Reacting to smoking cues

Between 70% and 90% of Americans with schizophrenia are smokers, yet treatments have had only modest success helping them quit. That effectiveness might be improved if more were known about what affects their smoking, including such environmental factors as smoking cues—for example, cigarettes, lighters, and ashtrays. Tidey and coauthors (p. 421) conducted what may be the first published study testing the effects of smoking cues on the urge to smoke and on negative affect among people with schizophrenia. They tested 25 outpatients’ reactions to both neutral and smoking-related objects, just after smoking and after 2 hours of abstaining, and found that exposure to smoking cues consistently increased smoking urge levels, despite differences in medications and symptoms. Abstaining from smoking did not appear to alter these effects.

The findings suggest that their model could be used to screen interventions that might be used to decrease reactions or exposure to smoking stimuli. The model might also be useful in investigating the neurobiological underpinnings of smoking urges among those with schizophrenia. In nonpsychiatric smokers, smoking cues activate brain regions associated with arousal, compulsive repetitive behaviors, sensory integration, and episodic memory—all brain regions functionally impaired by schizophrenia. “It seems likely,” the investigators write, “that qualitative or quantitative differences could exist between smokers with schizophrenia and matched nonpsychiatric smokers... [A] differential response to smoking cues could help to explain the heightened prevalence of smoking among people with schizophrenia.”

Women on the smokeless tobacco road

Only 0.5% of adult women in the United States currently use chewing tobacco or snuff, compared with 6.7% of men, but about 7% of adult women have tried smokeless tobacco at least once, putting them at heightened risk of trying it again. Because of women’s low rates of usage, risk factor studies have involved mostly men; it isn’t clear that the same factors predispose women to try smokeless tobacco. To learn more about which women are likely to try smokeless tobacco, Vander Weg and coauthors (p. 431) questioned 9,087 female recruits entering Air Force Basic Military Training. Of those, only 34 were still using smokeless tobacco, but 599 (6.6%) said they had tried it at least once. Other findings:

- Current smokers were almost four times more likely to have tried smokeless tobacco than were never-smokers.
- The odds of having tried it increased with frequent arguing, road rage, heavy drinking, and a host of other risk-taking behaviors, in patterns similar to those of men.
- Users were more likely also to have experimented with cigars, pipes, and other forms of tobacco.
- Contrary to other studies, use was lowest among recruits from the U.S. South, highest among those from the Midwest, followed by the West and Northeast.
- Unexpectedly, those with some post-high school education were more likely to have tried it than those without, although the odds ratio was modest.
- Native Americans and White women were more likely to have tried it than other racial groups, with Native Americans twice as likely as Whites.

The findings suggest that “elevated levels of anger, or perhaps a reduced ability to manage anger effectively, may be a characteristic” of women who experiment with smokeless tobacco, as well as “many of the characteristics commonly associated with sensation seeking.”

Carcinogens in Marlboro countries

The highest concentration of strong carcinogens in smoke from American-blended cigarettes consists of seven tobacco-specific nitrosamines (TSNAs). How do the cigarettes of other countries compare? Wu and colleagues (p. 443) explored these questions as the World Health Organization and the Centers for Disease Control and Prevention measured TSNA delivery in the smoke from cigarettes bought in the 10 most populous countries, three others, and the United States. The researchers found variations as broad as 35-fold. To compare TSNA levels, they machine-smoked a random cigarette from each of 15 packs of a locally popular brand bought in each country and a corresponding number of Marlboros also bought in that country, some made in the United States, some made in the host country. In the United States, domestic Marlboros were compared with the second most popular nonmenthol brand, Doral. It clearly mattered what brand was bought and where:

- Differences between Marlboros and local brands were significant everywhere except Mexico, Russia, and the United States.
- Marlboro consistently delivered more TSNAs than the local brand everywhere except Brazil, where the local brand delivered 1.5 more, primarily because Brazil’s Marlboros were two to three times lower in TSNAs than most others.

- In China, Marlboros delivered more than 30 times more TSNA's than the local brand. In Egypt, Marlboros delivered 1.5 times more.
- Compared to Marlboros sold in the United States, those in China, India, Kenya, and Pakistan delivered more TSNA's, and those in Brazil, Japan, and Mexico delivered less.
- Local brands sold in all other countries delivered less TSNA's than Doral.

The investigators also found good correlation between the amount of TSNA's found in the tobacco and what was delivered in its smoke, indicating that "the largest differences in carcinogenic TSNA levels...reflect primarily the different blending and curing practices in the manufacturing process." They also point out that new cigarette products promise to deliver less TSNA's, evidence that "it is now technically feasible for manufacturers to mass-produce cigarettes with reduced TSNA's."

Childhood ADHD: A road to quicker relapse

People who have attention-deficit/hyperactivity disorder (ADHD) tend to start smoking earlier, smoke more, and have more trouble quitting, possibly because nicotine improves ADHD symptoms, and withdrawal exacerbates them. In one of the first studies to examine associations between ADHD and smoking treatment outcomes, Humfleet et al. (p. 453) analyzed the results of two randomized trials that totaled 428 adult smokers who were given nicotine replacement, antidepressants, and psychological counseling. A history of childhood ADHD was diagnosed in 11% of the smokers. More of those relapsed than those with no such history, and they relapsed sooner:

- Only 1 of 47 smokers with childhood ADHD was still abstinent by week 52, compared with 18% of those without.
- Those with childhood ADHD relapsed after an average of 159 days, compared with 294 days for others.

The results mirrored baseline reports in which smokers with a history of childhood ADHD reported an average of 5 months abstinence in their most successful attempt, compared with an average of nearly 10 months for those without childhood ADHD. "This low success rate is particularly striking," the investigators report, "given that all participants received pharmacological or behavioral treatments known to be effective. Although the finding is limited by the small sample size, this result underlines the need to further evaluate smoking treatments for this high-risk group."

The data also suggest that nicotine replacement was more effective than nonnicotine treatments for

those with ADHD histories, but the small sample size precluded full examination of treatment-specific effects. Additional research should replicate the findings with larger samples of smokers with ADHD histories and should compare different treatment strategies.

Light smokers: Who are they, why they quit

One of every five smokers consumes five or fewer cigarettes a day, according to the Centers for Disease Control and Prevention, and their share of the smoking population is growing, yet relatively little is known about what sets them apart. Hyland et al. (p. 461) analyzed data from smokers in 22 communities in the Community Intervention Trial for Smoking Cessation (COMMIT) surveys in 1988, 1993, and 2001. They identified 13% as light smokers during at least one of the years. Among light smokers in 1988, and 38% had quit by 2001, compared with only 27% of heavier smokers who quit over the same period.

Compared with heavier smokers, light smokers tended to be female, unmarried, older, Black or Hispanic, and college educated; resided with no other adult smokers; and began smoking later in the day. Importantly, they were less likely to try quitting because of the cost of cigarettes or a physician's advice and more likely to try to quit so that they could set a good example, avoid contributing to secondhand smoke, or alleviate bad breath or tobacco odor. Although they used nicotine replacement products less, they were more likely to quit than heavier smokers. Also, they were more likely to smoke full-priced premium brands and to work in smoke-free worksites, suggesting that higher prices and worksite smoking restrictions might increase their number and encourage more smokers to quit.

These smokers, the investigators conclude, "may be motivated more by concern for others and aesthetics than by health reasons or advice from health care professionals," suggesting that interventions targeted at them "might include media campaigns that highlight the dangers of secondhand smoke or correlation between parental smoking and children smoking."

Dipping: How often, how long, not how much

Precancerous oral lesions are strongly associated with at least one of the two most potent carcinogens found in smokeless tobacco. Assessing levels of exposure to smokeless tobacco's carcinogens and the factors that contribute to that exposure is essential if the associated risks are to be reduced. Clearly, some brands are packed with more nicotine and carcinogens than others: Copenhagen and

Kodiak, the two best sellers, have the most; starter brands like Skoal Bandits have less. But does the way that tobacco is used, or the frequency and duration of “dipping” also play a role?

For 2 weeks, 54 adult male users of smokeless tobacco recorded in diaries each time they put a dip into their mouth, when they removed a dip from their mouth, and when a new tin was opened. When Lemmonds et al. (p.469) analyzed subjects’ urine samples, they found that the frequency and duration of use, but not necessarily the amount of smokeless tobacco they consumed, correlated strongly with nicotine and cotinine (biomarkers of tobacco exposure) and carcinogen metabolites. With every minute of increased average daily dipping duration, levels of urinary nicotine, cotinine, and metabolites of a carcinogen rose.

Of special concern, the authors note, average daily exposure in their study was about seven hours, much longer than the 4.2 and 4.7 hours found in earlier studies that had included younger users. Their findings suggest that smokeless tobacco users who want to reduce this exposure without quitting or changing brands should consider reducing not only the amount they use, “but more importantly, duration that [it] is kept in the mouth and frequency that they use the tobacco product. However, it is notable that to date, the only proven method for reducing health problems associated with [smokeless tobacco] use is no use at all.”

Smoking bans at drug treatment clinics

Almost everyone who seeks treatment for drug abuse is also a smoker, yet few drug abuse clinics treat nicotine dependence. Studies of the impact of smoking bans at health facilities have focused mostly on residential or inpatient facilities, but that

covers only 26% to 31% of U.S. drug treatment clinics. In what is believed to be the first survey of smoking policies in outpatient methadone maintenance clinics, Richter et al. (p.475) surveyed all 697 such clinics in the United States; 408 (59%) responded.

- Most had a written policy on patients (73%) and staff (82%) smoking; almost all of those with policies banned all indoor smoking.
- Having a written policy and restricting smoking were consistently tied to whether a clinic offered nicotine dependence treatment.
- Outdoors, about half the clinics restricted smoking to designated areas, while another 1 in 10 banned it altogether, leaving many that allowed patients (40.8%) and staff (35.2%) to smoke anywhere.
- Outdoor bans and restrictions were more common at public clinics, compared with private for-profit and nonprofit clinics, and among those attached to hospitals, compared with freestanding clinics or those attached to mental health organizations.
- Unaccredited clinics were less likely to have written smoking policies.

The authors note that most states reimburse facilities for their drug treatment services only if they satisfy certain mandates. “If smoking bans were mandatory, all facilities receiving reimbursement would have to comply,” they write. “Private, for-profit clinics are the fastest growing sector in methadone maintenance treatment ... [but they were] the least likely to restrict outdoor smoking ... [or] to provide nicotine dependence treatment. To address these discrepancies it may be necessary for methadone treatment regulations to explicitly require for-profit facilities to develop policies and treatments for nicotine dependence.”

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