Cessation of Smoking and Body Weight

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The health consequences of cigarette smoking are well established (1). Smoking has been linked to many serious health problems including cancer, coronary heart disease, stroke, and chronic obstructive pulmonary disease (2). As a result, smoking has been determined to be the single most preventable cause of death in Western society (3). Each year, an estimated 419,000 people in the United States die from smoking-related diseases (4), making it responsible for approximately one in every five deaths (2). Although overall smoking rates have declined over the past 30 years in the United States, nearly 26% of the population continue to smoke (5), including 3.1 million adolescents (6).

One of the many factors which may encourage smoking, despite health risks, is the influence of smoking on body weight. There is considerable evidence that the weight-controlling properties associated with cigarette smoking influence decisions to smoke. For example, the relationship between smoking and weight control has been linked to the initiation of smoking (7,8). In a study examining the relationship between weight concerns and cigarette smoking, French et al. (9) found that concerns about weight were associated with a greater likelihood of smoking initiation among female adolescents over a 1-year period. The relationship between smoking and body weight is also related to smoking maintenance in adults. Smoking for weight control is frequently reported, particularly by women (7,10,11). Additionally, individuals who are concerned about gaining weight are often more reluctant to quit smoking (12,13). Finally, concerns about gaining weight have been associated with failure to quit smoking (14,15) and relapse (7,16) although these effects appear to be equivocal (17–19).

WEIGHT DIFFERENCES BETWEEN SMOKERS AND NON-SMOKERS

It is well established that middle-aged and older smokers weigh less than comparably aged non-smokers. In a review of 29 cross-sectional studies evaluating weight and smoking status, smokers weighed an average of 3.4 kg less than non-smokers (1,20,21). Weight differences between smokers and non-smokers tended to be greater for moderate smokers (compared to light or heavy smokers), older smokers, and women (20). Although most studies have been conducted in American populations, similar weight differences between smokers and non-smokers (as well as a more pronounced weight-control effect for women compared to men) were reported from the World Health Organization MONICA project, which assessed weight and smoking status in 69,000 individuals from 42 populations (22).

This weight-attenuating effect of smoking, observed in adults after decades of smoking, is small or
non-existent in adolescent and young adult smokers. In a biracial sample of 6751 seventh grade students (average age of 13 years), daily smokers had a significantly higher body mass index (BMI) than non-smokers (21.61 vs. 20.56 kg/m², respectively) (23). Among 1926 members of this sample who were followed prospectively for 4 years, those who began smoking had greater increases in body weight for 2 years after initiation of smoking compared to non-smokers, especially white females after one year of smoking, and black males after 2 years of smoking. For those youths who smoked three or more years, body weight was virtually identical compared to those who never smoked (24). In a cross-sectional study of more than 31,000 young adult military recruits, smoking had no relationship to body weight in females, and a very small effect of body weight reduction in males, averaging less than 1 kg (25). Finally, Klesges et al. (26), in a 7-year prospective study of more than 4000 black and white young adults (18–30 years of age at baseline), reported that smoking produced a small attenuation of weight gain among Blacks (2.6 kg over 7 years, or 0.4 kg per year, adjusted for gender, baseline weight, age, education, physical fitness, alcohol intake, and fat intake). In contrast, smoking had no weight-attenuating effect among white men or women in this study, the latter being the group most likely to report smoking to control body weight (10). In summary, smokers weigh 3–4 kg less than non-smokers, on average, after many years of smoking. However, smoking has minimal impact on body weight in young smokers.

WEIGHT CHANGE AFTER SMOKING CESSATION

Smoking cessation reliably produces weight gain in both women and men, although the magnitude of this gain, and the mechanisms involved are less clear (20, 27). In the 1970s, a commonly reported but empirically unsupported estimate was that one-third of quitters gain weight, one-third remain the same, and one-third lose weight (28). Based on a review of 43 longitudinal studies, conducted primarily during the 1970s and 1980s, the average weight gain was estimated at 2.8 kg (0.8 to 8.2 kg) during the first year after cessation, with women tending to gain more than men (21). Another review around this time estimated post-cessation weight gain using only methodologically rigorous studies (1). Fifteen longitudinal investigations which included a control group of continuing smokers, a minimum follow-up length of 1 month, and a sample size of at least 10 quitters were examined. The average sample size of the reviewed studies was 1348 subjects with an average follow-up length of 2 years. The weight gain among quitters was considerably greater than that of continuing smokers (mean of 2.1 vs. 0.4 kg, respectively). Seventy-nine percent of quitters in this review experienced a weight gain (range of 58–87% among studies) compared to 56% of continuing smokers. Overall, the risk of weight gain after cessation was 45% greater for quitters compared to continuing smokers (RR = 1.45, CI = 1.31, 1.75). The prevalence of major weight gain (> 4.5 kg) was relatively low (20.3% vs. 0.8% for quitters and continuing smokers, respectively), but quitters were 90% more likely to experience major weight gain.

A large study of smoking cessation and weight gain in a national cohort (27) avoided several limitations common to previous studies, including short follow-up periods and reliance on self-reports of body weight. Subjects were more than 9000 participants in the First National Health and Nutrition Examination Survey (NHANES I) who were interviewed during the years 1971–1975 and re-interviewed during 1982–1984. Consistent with previous reports, women tended to gain more weight than men. The average weight gain attributable to smoking cessation (i.e difference in weight gain between quitters and continuing smokers), adjusted for age, race, education, alcohol, illnesses related to weight change, baseline weight, and physical activity was 2.8 kg for men and 3.8 kg for women. Major weight gain (> 13 kg) occurred in 9.8% of men and 13.4% of women. The relative risk of major weight gain for quitters, compared to continuing smokers, was 8.1 (CI = 4.4, 14.9) in men and 5.8 (3.7, 9.1) in women. Risk of major weight gain in women was greater for those who were initially underweight, younger (25–54 years vs. 55–74 years), physically inactive, and parous.

These NHANES I data also indicated that post-cessation weight gain was greater in Blacks than in Whites, with black women and black men being 3.3 times and 2.9 times more likely, respectively, to experience major weight gain compared to other ethnic groups (27). Similar ethnic differences were
observed recently in a 7-year prospective study of smoking and weight change among 5115 black and white young adults (26). Weight gain attributable to smoking cessation over a 7-year period in a large biracial cohort was 6.6 kg for Blacks compared to 4.2 kg for Whites. While 36.3% of white quitters experienced major weight gain (≥10 kg) over the 7-year follow-up, more than half of Blacks (52.3%) had major weight gain.

A prospective analysis of weight gain and smoking status among 121,700 nurses followed for 8 years (1976–1984) (29) found a mean attributable weight gain of 1.4 kg among quitters who had smoked <25 cigarettes/day and 2.8 kg for those who had smoked >25 cigarettes/day. Weight gain of 5 kg or more occurred in 14.2% of continuous smokers compared to 21.7% of women who had quit for less than 2 years. Consistent with the results of Williamson et al. (27), weight gain after cessation was positively associated with greater amount smoked, younger age, and initial lower weight.

Post-cessation weight gain does not appear to continue indefinitely, but causes weight to ‘catch up’ to that of non-smokers. Among both men and women in the NHANES I follow-up study reported by Williamson et al. (27) quitters weighed significantly less than never-smokers at baseline, but did not differ significantly after approximately 10 years of follow-up. Similarly, risk of major weight gain decreases over time. Williamson et al. (27) reported that for women, the odds of gaining >13 kg for sustained quitters, compared to continuing smokers, was 6.9, 8.8, and 4.2 for those quit 1 to 3 years, 4 to 6 years, and 7 to 12 years, respectively. For men, risk of major weight gain was 3.1, 11.8, and 7.9 for those quit 1 to 3 years, 4 to 6 years, and 7 to 12 years, respectively. In the Nurses’ Health Study, the incidence of 5 kg or more of weight gain was higher among women who had quit for ≤2 years compared to continuous smokers (21.7% vs. 14.2%), but incidence dropped to 16.0% and 17.1% among women quit for 2–4 years and 4–6 years, respectively. Among a cross-sectional study of more than 7000 Japanese workers (30), the risk of being overweight (BMI >25) was compared among former smokers and never-smokers. No differences in risk of being overweight were found between never-smokers and former light smokers (1–24 cigarettes/day) regardless of number of years quit. However, among former heavy smokers (≥25 cigarettes/day), those who had quit 2–4 years previously were nearly twice as likely to be overweight as never-smokers (OR = 1.88, 95% CI = 1.05–3.35) but no significant differences in risk of overweight between former and never-smokers were observed for those quit 5–7 years (OR = 1.32, CI = 0.74–2.34) or 8–10 years (OR = 0.66, CI = 0.33–1.31). Thus, smoking cessation, on average, causes weight to increase to levels typically experienced by non-smokers, and the risk of major weight gain also decreases as a function of time quit.

As noted above, available evidence from several prospective studies indicates that the magnitude of weight gain attributable to smoking cessation was on the order of 2 to 4 kg. There is reason to believe that these studies may have underestimated actual weight gain. One issue is that these estimates were based on studies conducted during the 1970s and 1980s. Individuals who have quit smoking in the past few years may be more nicotine dependent and have higher tobacco intake, two factors which increase the risk of post-cessation weight gain (27,29). Another issue is that few studies have been designed specifically to assess the effects of smoking cessation on weight gain prospectively and have relied on self-reports of smoking status and weight (1). In addition, studies have typically used point-prevalence estimates of smoking status rather than sustained abstinence. Two recent studies indicated that the magnitude of post-cessation weight gain may be higher than these previous estimates. Nides et al. (31) evaluated post-cessation weight gain in a sample of 691 sustained quitters from the Lung Health Study. Sustained quitting yielded weight gains 50–100% higher than the average weight gain reported in earlier studies (5.3 kg for women and 5.5 kg for men at the 1-year follow-up).

A recent study (32) compared the magnitude of weight gain using both point prevalence and sustained quitting definitions of abstinence. Subjects were 196 women and men followed prospectively for 1 year. Smoking status was validated biochemically and actual weights were obtained at each follow-up assessment. Those who met the criteria for point-prevalent abstinence (abstinent at the 1-year follow-up but no abstinence at one or more of the previous follow-ups) gained an average of 3.0 kg, which was very similar to previous estimates. However, subjects with sustained abstinence gained almost double this amount—5.9 kg. Thus, recent estimates of post-cessation weight gain, using more sophisticated methodologies, have indicated that
weight gain may be higher than previously estimated. It is common practice to advise smokers that the typical 2 to 3 kg post-cessation weight gain, while cosmetically unappealing, does not affect health status (29). However, if the average weight gain following smoking cessation is actually 6 kg, a substantially higher proportion of quitters than previously thought may experience major weight gain.

MECHANISMS OF POST-CESSATION WEIGHT GAIN

The exact mechanisms underlying post-cessation weight gain still are not well understood. According to the principles of energy balance, smoking cessation must lead to either an increase in energy intake, and/or a decrease in energy expenditure (viz., metabolic rate, physical activity) to promote weight gain (33).

Physical Activity

The available data indicate that physical activity does not play a role in the relationship between smoking and body weight (20,33,34). Cross-sectional studies comparing activity levels in smokers and non-smokers have failed to find discrepancies that would account for the difference in body weight between the two groups (20,35). In fact, studies finding a relationship between smoking status and physical activity have typically found smokers to be less active than non-smokers (36–38). Additionally, physical activity does not appear to decrease following smoking cessation (33,39–41). Those studies finding changes following smoking cessation have reported increases in physical activity (42–44). Thus, physical activity does not appear to figure independently in either the difference in body weight between smokers and non-smokers, or in post-cessation weight gain.

Dietary Intake

Energy intake appears to play an important, although complicated, role in the relationship between smoking and body weight (34). Despite the fact that they tend to have lower body weights, smokers consume as much, or more energy than non-smokers (37,45,46).

Additionally, smoking cessation is associated with increased energy intake, at least acutely. Several studies of short-term cessation (1 day to 7 weeks) have documented increases in total energy (41,47–49) although negative findings also have been reported (39,43,50). Despite considerable variability in methodology, studies typically show an immediate increase in energy intake of 250 to 300 kilocalories per day following smoking cessation (51,52).

Long-term changes in intake following smoking cessation, however, have been less consistent (52). Unfortunately, few studies have examined changes in energy intake beyond a few months post-cessation. One study, however, assessed changes in dietary intake among women who quit smoking for a period of 1 year. Caan et al. (53) found increases of 163 and 125 kcal/day at 1 and 6 months post-cessation, respectively. Levels of energy intake had returned to baseline, however, by the 1-year follow-up. These results suggest that increases in energy intake following smoking cessation probably do not extend much beyond 6 months, which may help to account for the fact that most of the weight that is gained after quitting smoking occurs within this time period (32,53–55).

In addition to short-term increases in total energy intake, smoking cessation has been associated with changes in specific components of dietary intake. Selective increases in dietary fat (56), carbohydrates (57), sucrose (56,58), and alcohol (41) have been observed following smoking cessation. Overall, increases in dietary intake after smoking cessation appear to be due to between-meal snacking, rather than from a general increase in food consumption during meals. Gilbert and Pope (59) found that energy intake from meals was similar during 24-hour periods of ad libitum smoking and abstinence, but that intake from between-meal snacks increased 50% in men and 94% in women during abstinence.

Given that women generally have greater concerns about post-cessation weight gain, as well as greater actual weight gain, gender differences in the mechanisms of post-cessation weight gain are of major interest. There is evidence that changes in energy intake associated with smoking cessation may differ by gender, but the exact relationship is
unclear. While several studies have reported differences in energy intake as a function of gender, they have disagreed on the nature of the relationship. Klesges et al. (39), for example, found increased intake of polyunsaturated and monounsaturated fat in women during a week of abstinence, but no changes in dietary intake for men. Conversely, Hatsukami et al. (60) observed a greater increase in total energy intake in men than women following 4 days of cessation. Hall et al. (56) found that both women and men increased their intake of total energy, fat, and sucrose immediately after quitting. Men decreased their average total energy intake by nearly 1000 kcal from the first week after cessation to 4 months (3014 to 2119 kcal) and maintained this lower level at 6 months (2035 kcal). In contrast, total energy intake by women remained stable (1841, 2077, and 1867 kcal at 1 week, 4 months, and 6 months, respectively). Increased energy intake predicted weight gain at 6 months for women, but not for men. Thus, information on the influence of gender on changes in energy intake following smoking cessation is incomplete, but suggests significant and sustained post-cessation energy intake increases in women, which are associated with weight gain.

**Metabolic Rate**

Studies examining the relationship between smoking and metabolic rate have been inconclusive. There is considerable indirect evidence that metabolic factors influence the weight-controlling properties of smoking. The fact that smokers are no more active than non-smokers and consume as much or more energy, yet weigh less, suggests that metabolism may play a role in the relationship between smoking and body weight (34).

Several studies have documented acute metabolic increases due to smoking or nicotine administration (61–64). At least one study did not find any acute effect of smoking on metabolic rate (65) and in general, there appears to be tremendous individual variation in the metabolic response to smoking and smoking cessation (1,62). There is evidence that the acute effects of smoking may be more pronounced during light physical activity than during rest (63,66), at least among men, and for normal weight smokers than the obese (61). Thus, it is possible that the acute metabolic effects of smoking may factor into the difference in body weight between smokers and non-smokers, although it remains unclear whether these effects are strong and persistent enough to have a substantial impact on body weight.

Studies that have directly examined the chronic metabolic effects of smoking have produced inconsistent results. Cross-sectional studies comparing resting energy expenditure (REE) in smokers and non-smokers have typically found little or no differences between the groups (38,67). The few studies that did find differences failed to control for the thermic effects of nicotine by allowing smokers to smoke before the assessments, which could have resulted in an overestimation of the chronic effects of smoking on metabolic rate (68).

Only a few prospective studies have examined metabolic changes during long-term smoking cessation, and conflicting results have been found. Moffatt and Owens (40) compared changes in metabolic rate among 36 women who quit for 60 days (n = 12), quit but relapsed 30 to 60 days post-cessation (n = 6), continued smoking (n = 8), or were non-smokers (n = 10). Resting metabolic rate (RMR) was assessed as oxygen uptake at baseline, 30 and 60 days post-cessation. At baseline, RMR was higher in smokers than non-smokers. No changes in RMR were observed for non-smokers or continuing smokers. Smoking cessation resulted in a 16% decrease in RMR at day 30. Both relapsers and abstinent subjects showed trends for RMR to rebound toward baseline at day 60. Despite the trend for RMR to return toward baseline, weight continued to increase throughout the 60-day follow-up. The authors estimated that 39% of the weight gain among quitters was attributable to change in RMR. Dallosso and James (50) reported a 4% decrease in resting metabolic rate following smoking cessation, although the change was only significant when expressed per kilogram of body weight.

In contrast, Stamford et al. (49) did not find changes in oxygen consumption in 13 subjects who quit smoking for 48 days. Additionally, a recent study (69) assessed 24-hour energy expenditure in a respiratory chamber and basal metabolic rate among eight smokers (four men and four women) during regular smoking and after 4 to 8 weeks of abstinence. No significant differences were observed between smoking and non-smoking assessments for
either measure of energy expenditure, suggesting that smoking cessation does not produce any chronic alteration in metabolic rate. Other studies also have failed to find chronic changes in resting energy expenditure (REE) after quitting smoking (70–72). Thus, the relationship between smoking and REE remains unclear. One possible explanation is that changes in REE following smoking cessation are influenced by moderators, such as ethnicity or gender. Most studies investigating this relationship have consisted of small, homogeneous samples, making it impossible to investigate these variables. Thus, there is a need to examine changes in REE following smoking cessation in large, diverse samples.

Simultaneously examining the influence of all three energy balance variables would be helpful in understanding the relative contribution of each component. However, to date, only five prospective studies have examined the influence of smoking cessation on all three components of energy balance. Four of these studies utilized relatively short follow-up periods (14 to 60 days). Vander Weg et al. (73) examined changes in energy balance in 95 male and female smokers during 2 weeks of abstinence from smoking. Energy intake increased significantly following cessation (344 kcal/day). There were no changes, however, in REE or physical activity. Stamford et al. (49) examined changes in body weight and energy balance in 13 women following 48 days of abstinence from smoking. There were no changes in either physical activity or REE. Energy intake, however, did increase by an average of 227 kilocalories/day. Perkins et al. (41) investigated changes in energy balance in seven female smokers over a 3-week period consisting of a week of smoking, a week of abstinence, and a return to smoking. Energy intake increased significantly during the week of abstinence, primarily due to an increase in alcohol consumption. REE also changed over the 3-week period. A non-significant decrease in REE was observed during abstinence, followed by a significant increase upon return to smoking. There were no changes in physical activity. Finally, Moffatt and Owens (40) examined changes in energy balance in 18 women who quit smoking for 30 to 60 days. Consistent with the other studies, physical activity did not change as a function of smoking status, while energy intake increased significantly following cessation. However, unlike the three previous studies, smoking cessation was associated with a significant decrease in REE.

Klesges et al. (55) assessed the relationships of all three major components of energy balance and weight gain during 12 months of abstinence—the longest follow-up period to be examined to date. The sample included 42 subjects (22 women, 20 men) with biochemically verified sustained abstinence over the 12-month following period. Weight gain among women was predicted by lower baseline REE, higher baseline total energy intake, and increased carbohydrate intake over the year. However, changes in energy balance components (dietary intake, physical activity, and REE) did not predict weight gain among women. Furthermore, no energy balance variables predicted weight gain for men. Future research should attempt to examine more fully potential gender differences in energy balance changes that predict weight gain during extended smoking cessation.

In summary, increases in energy intake appear to be the most consistent energy balance change following smoking cessation. There is no evidence that changes in physical activity generally contribute to post-cessation weight gain. While removal of the acute increases in metabolic rate caused by smoking may also contribute somewhat to post-cessation weight gain, long-term changes in metabolic rate after smoking cessation do not occur reliably.

PREVENTION OF POST-CESSATION WEIGHT GAIN

Numerous behavioral and pharmacologic interventions have been developed during the past 10 years in an attempt to reduce or prevent post-cessation weight gain (see reviews by Perkins et al. (74); Perkins (75)). These efforts may seem misguided given that weight gain after quitting smoking is rather modest (typically not higher than 6 kg, on average) and less health-damaging than continued smoking. Furthermore, the actual amount of weight gain has been shown to be unrelated to outcome in some studies (76,77) or to predict continued abstinence in others (54). However, as discussed above, many smokers, particularly women, report using smoking as a weight-control strategy, and fear of gaining weight as a reason for not attempting to quit. As such, adjunct treatments that effectively address these concerns clearly are needed to optimize
smoking cessation interventions. Below, both behavioral and pharmacologic strategies will be described.

**Diet and Exercise Interventions**

Because of the evidence that most of the cessation-induced weight gain is due to increased eating, it has been widely accepted that efforts to prevent this weight gain through dieting will improve abstinence. However, there is little direct support for this assumption and some evidence supporting the opposite notion, that attempting to prevent moderate weight gain after quitting may be detrimental. Hall *et al.* (78) supplemented an intensive behavioral smoking cessation program (seven 1 1/2 hour sessions over 2 weeks) with either (1) a behavioral weight control program (five sessions over 4 weeks consisting of daily weight and calorie monitoring, encouragement to engage in aerobic exercise ≥ 3 times per week, and behavioral self-management principles, (2) a non-specific weight control program (group therapy providing support and information on diet and exercise), or (3) standard treatment control (a printed information packet on nutrition and exercise). Unexpectedly, subjects in both weight control conditions had lower abstinence rates at end of treatment and 1 year follow-up than those in the standard treatment. Also, weight gain was not attenuated in either of the weight control conditions relative to standard treatment, at either 6 weeks or 1 year post-treatment.

Pirie *et al.* (79) randomized 417 female smokers in a 2 × 2 design to receive nicotine gum vs. no gum crossed with weight control counseling vs. no weight control counseling. All four groups received behavioral smoking cessation counseling. Weight control counseling involved counseling to modestly reduce caloric intake and increase activity. At 12 months, abstinence rates were highest among subjects receiving nicotine gum only, and lowest in those who received nicotine gum plus the weight control programs.

Results from both of these large, well-conducted investigations suggest that adding a weight control component to an already intensive smoking cessation intervention provides too complicated an approach that overwhelms participants. Attempts to focus one’s attention simultaneously on weight control and smoking abstinence may actually lead to failure to accomplish either. Another possible reason for the failure of these interventions to prevent weight gain is that reducing energy intake may lead to the loss of another powerful reinforcer (in addition to nicotine), which in turn encourages smoking. Consistent with this hypothesis is that food deprivation increases the self-administration of several drugs in animals, including nicotine (74). It may also be that eating helps to attenuate nicotine withdrawal symptoms (74). This is consistent with the results of two studies that have found that both food (80) and glucose tablets (81) reduced cravings for cigarettes during abstinence from smoking.

If the failure of these interventions to prevent weight gain is due to cognitive overload from simultaneously trying to change two behaviors, then delaying the weight control intervention until after smoking cessation had been achieved would be expected to prevent weight gain more effectively. This hypothesis is supported in preliminary data from 291 women enrolled in a 16-week behavioral smoking cessation/weight gain prevention trial (82). Subjects were randomized to receive the weight control intervention early in the program (first 8 weeks), late in the program (last 8 weeks), or to no weight control component. Although cessation outcomes did not differ among the three groups, at both 6 and 9 months post-cessation, subjects who received the weight control intervention late gained less weight than either control subjects or those who received the intervention early. These data suggest that a behavioral intervention can reduce post-cession weight gain, without undermining smoking cessation, by delaying the weight management component.

Although promoting adherence to regular physical activity is challenging, there is evidence that incorporating physical activity into smoking cessation interventions can reduce post-cessation weight gain. In a prospective observational study of 9306 nurses who were regular smokers at baseline, change in weight over 2 years was evaluated as a function of changes in smoking status and physical activity levels. Among women smoking 1–24 cigarettes/day at baseline, those who quit without changing their exercise level gained an average of 2.3 kg more than women who continued to smoke. In contrast, women who quit gained an excess of only 1.8 kg if they increased exercise by 8–16 MET-hours/week (equivalent to 1–2 hours of vigorous
activity/week), and only 1.3 kg if they increased exercise by more than 16 MET-hours/week (83).

A recently published clinical trial randomized 281 sedentary women to receive either a 12-week behavioral smoking cessation program with either vigorous aerobic exercise (three 1-hour supervised sessions of aerobic activity per week for 12 weeks) or an equal time contact control condition (health education lectures and discussions) (84). At the end of treatment, subjects in the exercise condition gained less weight than control subjects (3.05 vs. 5.40 kg, respectively). However, the groups did not differ in the magnitude of weight gain at 12 months follow-up. Unfortunately, only 10% of subjects in the exercise condition continued with regular exercise throughout the 1-year follow-up period. Thus, while exercise appears to be a helpful strategy to prevent post-cessation weight gain, longer treatment periods probably are needed to sustain its effect. It is likely, however, that such an intensive approach is not appealing to many smokers. In this study, a high proportion (68%) of eligible smokers chose not to participate, and substantial loss to follow-up occurred.

Perkins et al. (74) have argued that weight gain early after cessation, even if somewhat attenuated by a weight control intervention, may be enough to discourage continued efforts to remain abstinent. While there is clear evidence that integrating a weight control component into smoking cessation interventions can attenuate weight gain, these programs have not entirely prevented weight gain. However, one study indicates that behavioral change is capable of entirely preventing weight gain, albeit in highly controlled circumstances (military boot camp) (85). Participants were 332 Air Force recruits (227 men, 105 women) undergoing 6 weeks of basic military training. A total ban on smoking was strictly enforced throughout training, and recruits underwent a rigorous program of strenuous daily physical activity (aerobics, calisthenics, drilling, marching, etc.) and ad libitum access to food at meals but no access to snack foods or between-meal eating. At the end of training, all recruits tended to lose weight, although non-smokers lost marginally more than did smokers (0.89 vs. 0.03 kg, respectively, \( P = 0.07 \)). Thus, under an ‘ideal’ treatment environment involving increased physical activity and prohibition of snacking, post-cessation weight gain can be eliminated.

Given that post-cessation weight gain tends to be modest and does not predict success at quitting, Perkins (74) has suggested treating weight concerns rather than weight gain per se, as a potentially useful intervention. Perkins and colleagues are testing this hypothesis in an ongoing clinical trial, where a cognitive–behavioral intervention is used to challenge attitudes and perceptions regarding weight and body image. The goals of the intervention are to tolerate a modest increase in snacking and not to overreact emotionally to a modest weight increase.

**Pharmacologic Interventions**

Several pharmacologic strategies to prevent post-cessation weight gain have been evaluated, including nicotine replacement, and both serotonin-enhancing and catecholaminergic drugs. Several clinical trials have found that nicotine gum attenuates post-cessation weight gain, at least during treatment (77, 86–88). Furthermore, these effects appear to be dose-dependent (86, 88). For example, Doherty et al. (86) examined weight gain through 90 days post-cessation among 79 abstinent cigarette smokers who were randomized to either placebo or 2 mg or 4 mg of nicotine gum. Nicotine gum was shown to suppress weight gain in a dose-dependent fashion. At 90 days post-cessation, placebo gum users gained 3.7 kg, compared to 2.1 kg and 1.7 kg for subjects receiving 2 mg and 4 mg of nicotine gum, respectively. A similar dose-dependent effect on weight gain was observed when the percentage of baseline cotinine levels replaced during treatment was correlated with weight gain.

Unfortunately, the weight-control benefits of nicotine gum appear to persist for only as long as the gum is used. Among patients treated with 2 mg nicotine gum in a hospital-based smoking cessation clinic, those who quit successfully for one year gained less weight if they continued to use the gum throughout the year (mean weight gain of 3.1 kg) compared to successful quitters who discontinued use of the gum (5.2 kg) (87).

In contrast to nicotine gum, the weight-attenuating effects of transdermal nicotine (‘the patch’) have been less consistent. In a quantitative review of four clinical trials, both placebo and transdermal nicotine groups gained weight during the periods of study, with no differences between conditions (89).
Several other studies, however, have reported reduced weight gain among patients treated with transdermal nicotine relative to placebo. For example, Abelin et al. (90) randomized patients to transdermal nicotine or placebo. After 3 months, those in the placebo group gained 4.4 kg, compared to only 0.1 kg in those receiving active treatment. Jorenby et al. (91) also examined post-cessation weight changes among patients randomized to 21 mg transdermal nicotine or placebo. Those treated with transdermal nicotine gained significantly less weight after 4 weeks (1.85 kg) than those receiving placebo (2.88 kg). Finally, Allen et al. (92) compared post-cessation weight changes among participants receiving three doses of transdermal nicotine (7, 14 and 21 mg) or placebo. Weight changes after 6 weeks were 2.5 kg (placebo), 2.03 kg (7 mg), 1.98 kg (14 mg), and 1.85 kg (21 mg), with those receiving 21 mg of transdermal nicotine gaining significantly less weight than those assigned to placebo. Thus, while some studies have reported transdermal nicotine to be associated with reduced post-cessation weight gain compared to placebo, others have found no weight attenuating effects.

Perkins (75) proposed three possible explanations for the weight-gain-attenuating benefits of nicotine gum compared to the patch. First, the differing route of administration of gum allows gum to produce more variable change in blood nicotine levels and allows for self-titration of dose. Second, the sensory and/or behavioral effects of nicotine gum may be incompatible with or otherwise discourage eating. Third, self-selection of subjects may occur in studies utilizing nicotine gum vs. patch. Nicotine gum places greater behavioral demands on subjects (in terms of frequency of chewing, following behavioral instructions) which may be related to motivational level or ability/willingness to perform other behaviors necessary to prevent weight gain.

Another possibility is that the typical doses of nicotine obtained from the patch may be insufficient to reduce weight gain. Transdermal nicotine has been found to reduce post-cessation increases in total energy, carbohydrate, and fat intake in a dose-dependent fashion (93). Additionally, in a clinical trial comparing three dosages of transdermal nicotine (11, 22, 44 mg/day) among 70 subjects, weight change over 8 weeks of patch use was negatively correlated with percentage of cotinine replacement ($r = -0.38$, $P = 0.012$) (94). Unfortunately, no studies have directly compared the weight-gain-attenuating effects of nicotine gum vs. patch at equivalent doses. One clinical trial, however, compared a combination of nicotine gum and nicotine patch (combined condition) vs. nicotine gum and placebo patch (gum only), used for 18 weeks (95). At 12 months post-treatment, weight gain was attenuated in subjects in the combined condition compared to those in the gum only condition (2.7 kg vs. 4.0 kg, respectively). Although the percentage of cotinine replaced was not measured in the study, the greater weight attenuation in the combined condition suggests a weight control benefit to the patch, possibly due to greater total dosage of nicotine replacement. Collectively, these findings suggest that the amount of nicotine that is replaced, rather than the method of administration, may have the greater impact on post-cessation weight gain.

Two newer nicotine replacement products, a nasal spray and an inhaler, have recently become commercially available in the United States. Similar to results with gum and patch, nicotine nasal spray has been shown to attenuate weight gain, but only during the period of usage. Sutherland et al. (96) randomly assigned 227 smokers to 4 weeks of group supportive treatment plus either active nicotine spray or placebo nicotine spray. Recommended duration of nasal spray usage was 3 months, but subjects were allowed to continue use beyond this time. At 12 months post-cessation, those in the placebo spray condition gained an average of 5.8 kg. Weight gain among those subjects in the active spray condition who discontinued use of spray at the end of the treatment period was similar to placebo subjects (5.5 kg). In contrast, subjects who were still using the active spray at the 12-month follow-up gained only 3.0 kg.

Two placebo-controlled clinical trials of the nicotine inhaler have examined short- and long-term effects on weight gain. Tonnesen et al. (97) found no difference in weight gain between conditions at either 6 weeks or one year post-cessation. Another study, however, found non-significant trends for the inhaler, compared to placebo inhaler, to attenuate weight gain at 2 weeks post-cessation (0.6 kg vs. 1.2 kg, respectively, $P = 0.07$) and 12 months post-cessation (4.5 kg vs. 5.6 kg, respectively, $P = 0.09$) (98).

Other studies have examined non-nicotine pharmacologic strategies to prevent weight gain. Phenylpropanolamine (PPA), a catecholaminergic...
drug, has been found to prevent weight gain completely during 2 weeks of smoking abstinence (99). Over 4 weeks of cessation, PPA was shown to reduce weight gain by more than 50% (100). Thus, while PPA shows promise as an adjunct pharmacologic treatment to prevent post-cessation weight gain, no published studies have yet evaluated its long-term efficacy.

A few studies have evaluated the effects of dexfenfluramine and fluoxetine, both serotonin-enhancing drugs, on post-cessation weight gain. In a study of 31 overweight female smokers, Spring et al. (57) demonstrated that dexfenfluramine prevented weight gain (and actually led to a small weight loss, averaging 0.8 kg) during 4 weeks of smoking abstinence compared to placebo. In another small, short-term clinical trial, fluoxetine was shown to prevent weight gain entirely (mean weight change = −0.6 kg) compared to placebo (3.3 kg increase) among smokers who significantly reduced their nicotine intake (101). Spring et al. (102) compared the efficacy of dexfenfluramine and fluoxetine in preventing post-cessation weight gain. Subjects were 144 normal weight women, randomized to dexfenfluramine (30 mg), fluoxetine (40 mg), or placebo for 14 weeks. At 1 month post-cessation the placebo group gained more weight than either of the drug groups. By 3 months post-cessation the dexfenfluramine group had gained significantly less weight (1.0 kg) compared to either the placebo (3.5 kg) or fluoxetine (2.7 kg) groups. By 6 months post-cessation, however, weight gain was similar among the three groups. Both of these studies suggested that the weight-gain-attenuating effects of serotonin-enhancing drugs was related to suppression of the usual increases in energy intake observed after smoking cessation, particularly carbohydrates.

A recent study (103) compared the effects of two dosages of fluoxetine (30 mg vs. 60 mg) to placebo on post-cessation weight gain. During treatment, weight gain among placebo subjects was greater (2.61 kg) than that of subjects receiving either 30 mg of fluoxetine (1.33 kg) or 60 mg (1.25 kg). However, after discontinuing the drug, subjects who received 60 mg of fluoxetine had greater weight gain (6.5 kg) than subjects receiving either 30 mg of fluoxetine (3.6 kg) or placebo (4.7 kg). Thus, similar to the effects of nicotine replacement, serotonergic drugs minimize post-cessation weight gain, but only for the duration of drug treatment. Unfortunately, however, the observed dose-dependent weight rebound after discontinuation of fluoxetine indicates the drug may have limited utility for the long-term prevention of post-cessation weight gain.

Two recent studies examined the effect of bupropion on post-cessation weight gain. Hurt et al. (104) compared weight gain among patients treated for 7 weeks with three doses of bupropion (100, 150, and 300 mg) or placebo. Weight change was found to be negatively associated with dose following 6 weeks of cessation. Weight gain among those receiving placebo averaged 2.9 kg, compared with 2.3 kg among those receiving either 100 or 150 mg of bupropion, and 1.5 kg for those in the 300 mg group. No group differences in weight gain, however, were observed at the 6-month follow-up. Jorenby et al. (105) examined post-cessation weight changes among participants in a 2 (300 mg bupropion vs. placebo) × 2 (transdermal nicotine patch vs. placebo) randomized clinical trial. Those in the combined treatment group (i.e. bupropion plus transdermal nicotine) gained significantly less weight at 6 weeks (1.1 kg) than those in either the bupropion only (1.7 kg) or double placebo (2.1 kg) groups, and a similar but non-significant trend was observed for the patch-only group (1.6 kg). No differences in weight gain among treatment groups existed at 6 months follow-up, however. Thus, while bupropion may help to reduce post-cessation weight gain in the short term, the weight-attenuating effects do not appear to last beyond the duration of treatment.

CONCLUSIONS

It is clear that smokers weigh less than non-smokers (averaging 3 to 4 kg) after many years of smoking. However, among adolescents and young adults, weight differences between smokers and non-smokers are small or non-existent, and smoking initiation is not associated with weight loss. In contrast, smoking cessation reliably produces weight gain. In several large prospective studies, weight gain attributable to smoking cessation has averaged 2 to 4 kg, and has been greater in women, Blacks (compared to Whites), younger smokers, those who weigh less prior to quitting, and those who smoke more (27,34). On average, quitting smoking increases one’s weight to a level that would be ex-
pected for a non-smoker. Although some individuals experience major weight gain (10 kg or so) after quitting smoking, this occurs in a relatively small proportion of quitters—generally fewer than 20%. Post-cessation weight gain seems to be largely related to increases in energy intake, particularly high fat and carbohydrate between-meal snacking (74). Loss of the acute metabolic-enhancing effects of nicotine may also partly contribute to weight gain, but the bulk of evidence argues against a chronic effect of smoking cessation on metabolism (33).

It may seem ironic that there currently is so much interest in developing smoking cessation interventions that effectively reduce or eliminate post-cessation weight gain, given that weight gain generally is modest, and is certainly less health-damaging than continued smoking. However, many smokers, particularly women, have serious concerns about post-cessation weight gain which contribute to decisions not to attempt quitting, or to relapse once cessation has been attempted (74). As such, cessation interventions that are effective at preventing weight gain may encourage smokers to quit, and may provide additional motivation to remain quit. Behavioral strategies involving restriction of energy intake and increased physical activity generally have failed to prevent weight gain, and have also impeded cessation efforts, possibly because individuals become overwhelmed at changing two behaviors simultaneously. Staggering the interventions, such that weight control efforts are not attempted until smoking cessation is firmly established, shows promise of attenuating weight gain (82). Additionally, several pharmacologic interventions, including nicotine replacement and serotonergic and catecholaminergic agents, have been shown to reduce post-cessation weight gain, although this effect is limited to the duration of drug treatment. More work is needed to improve the efficacy of both behavioral and pharmacologic approaches to reduce post-cessation weight gain, and combining behavioral and pharmacologic strategies may be a promising approach to eradicating this tenacious problem.

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