Naltrexone Reduction of Long-Term Smoking Cessation Weight Gain in Women But Not Men: A Randomized Controlled Trial

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Background: The opioid antagonist naltrexone has shown promise to reduce weight gain during active treatment, but longer-term studies have not been conducted. The goal was to examine effects of naltrexone on weight gain over long-term follow-up in men and women who quit smoking.

Methods: Weight was examined at baseline and 6- and 12-month follow-up in the two largest randomized, double-blind, placebo-controlled trials of naltrexone in nicotine dependence. For 6–12 weeks after the quit date, participants were randomly assigned to receive naltrexone or placebo. Behavioral counseling and open-label nicotine patch were also included for the first 4–6 weeks. Of the 700 participants in the combined intent-to-treat sample, there were 159 (77 women) biochemically verified abstinent smokers at 6 months, and 115 (57 women) of them remained abstinent at 12 months. Changes in weight (in kilograms or in percentage) and body mass index from baseline to the follow-ups were assessed for these participants.

Results: Weight gain was significantly lower for women treated with naltrexone compared with placebo (6 months, 3.3 vs. 5.5 kg; 12 months, 5.9 vs. 7.4 kg, respectively). Increases in body mass index and percentage body weight gain were also significantly lower in women treated with naltrexone versus placebo. These effects were not observed in men.

Conclusion: The results provide evidence for naltrexone as the first pharmacotherapy to reduce postsmoking cessation weight gain among women.

Key Words: Naltrexone, nicotine dependence, opioid antagonist, sex differences, smoking cessation, weight gain

Most adults in the US currently are either overweight (34.4%) or obese (33.8%), and rates continue to increase steadily (1). Obesity is second only to tobacco use as the leading cause of preventable death in our country (2). Ironically, the most common adverse effect of smoking cessation is weight gain, which is observed in more than 80% of persons who are successful in quitting smoking (3). The average weight gain 6 months after the quit date is usually between 2.3 and 4.5 kg (4), but a sizeable portion of smoking abstainers (10%–25%) gain more than 6.8 kg (5). On average, women gain more weight than men (5) and experience greater concern and distress about gaining weight (6), which might deter them from attempting or continuing with a quit attempt (7).

To date, numerous approaches have been examined for reducing weight gain in the treatment of tobacco dependence. The recent 2012 Cochrane Report evaluating interventions to prevent weight gain after smoking cessation concluded that, although some exercise behavioral management strategies and approved pharmacotherapy approaches such as varenicline, nicotine gum, and bupropion might delay weight gain, none were effective 6 or more months after cessation or evidence was insufficient to support them for clinical recommendations in prevention of cessation weight gain (4).

Of the novel pharmacological treatments studied thus far to reduce postcessation weight gain, the Cochrane Report concluded that the most promising results have been obtained with the μ opioid receptor antagonist naltrexone. However, they noted that evidence was lacking on long-term weight gain effects of naltrexone after the medication is stopped. During treatment intervals ranging from 4 to 12 weeks, naltrexone has been shown to significantly reduce weight gain on average by 1 to 1.5 kg relative to placebo (8–11), and effects might be stronger in women compared with men (9,12). The only published study of longer-term weight gain examined low-dose naltrexone (25 mgdaily) for 6 months in weight-concerned smokers; results showed that naltrexone reduced weight gain (3.1 vs. 4.4 kg with placebo), but this difference was not statistically significant (13). This might have been due to the recruitment of a particularly treatment-resistant smoker subgroup with little tolerance for weight gain, high attrition with only 34% completing treatment, and the low dosage, which might not have produced adequate inhibition of μ opioid receptors, as has been shown with 50 mg (14).

The mechanisms underlying weight gain post cessation in smokers are complex but most likely the result of heightened food reward (15) and increased intake of palatable food with high sugar and fat content (16), because changes in metabolic rate likely play a lesser role (17). The endogenous opioid system might represent a good biological target, because it is involved in food hedonics and eating behaviors (18–20). A competitive opioid antagonist such as naltrexone might affect opioidergic pathways and their connections to midbrain dopamine circuitries involved in the motivational and hedonic aspects of feeding behavior (21,22). Effects of naltrexone on weight gain over time is plausible even after the drug is discontinued, because greater food reward

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and high calorie food intake during the first few weeks of cessation predict longer-term weight gain, particularly in women (16). Alteration of opioid-mediated neurobiological processes involved in excess calorie intake during this early period might be crucial in reducing weight gain over time.

The purpose of this study was to compare weight gain at 6- and 12-month follow-up in women and men smoking abstainers who were randomized to naltrexone or placebo for up to 3 months of smoking cessation treatment. Participants were extracted from a combined sample of the two largest randomized, placebo-controlled clinical trials to date examining the efficacy of naltrexone (9,11). Briefly, both studies showed some support for naltrexone to increase quit rates and reduce smoking urge during acute treatment of 6–12 weeks (9,11). Both studies also demonstrated that naltrexone reduced weight gain during active treatment. Less than one-quarter of the participants in either study remained biochemically confirmed as abstinent at the follow-ups, as observed in most smoking cessation trials (23). Therefore, analysis of the longer-term effects of naltrexone on weight gain, particularly examination of potential sex differences in this response, was not possible in the individual trials. By combining these studies, we herein provide the first examination of naltrexone on long-term cessation weight gain. Abstainers were the primary focus to avoid heterogeneity with nonabstainers who usually do not gain weight or lose the weight they had gained during initial abstinence (4). We predicted that naltrexone compared with placebo would significantly reduce the amount of weight gained as well as the increase in body mass index (BMI), percentage increase in body weight, and incidence of clinically significant weight gain defined as 7% baseline body weight gain. This latter criterion is reported as an adverse event in product labeling approved by the U.S. Food and Drug Administration and is a widely used index for measuring unwanted weight gain from use of psychiatric medications (24–26). We also predicted that these effects would be more pronounced in women than in men.

Methods and Materials

Participants

Participants were extracted from the two randomized, placebo-controlled clinical trials examining the efficacy of naltrexone in general adult smokers seeking treatment for nicotine dependence at the University of Chicago (9) and Yale University (11). The total intent-to-treat sample included 700 smokers, with 315 participants from the Chicago sample and 385 participants from the Yale sample (consort diagram in Supplement 1). At 6-month follow-up, there were 159 smokers (22.7%) who reported being smoke-free over the past 7 days and provided biochemical verification (i.e., ≤10 ppm on an expired air carbon monoxide breath test). These included 82 participants from Chicago (40 in the placebo group, 42 in the naltrexone group [dose: 50 mg]) and 77 participants from Yale (20 in the placebo group, and 57 in the naltrexone group [25 mg, 20 participants; 50 mg, 15 participants; 100 mg, 22 participants]). There were 115 smokers (72% of the 6-month abstainers) who remained biochemically confirmed as abstinent at the 12-month follow-up, with 58 from Chicago (33 placebo, 25 naltrexone) and 57 from Yale (15 placebo, 42 naltrexone group [25 mg, 11 participants; 50 mg, 11 participants; 100 mg, 20 participants]).

Participants were enrolled in the trials from July 2006 to March 2008 (Chicago) and November 2000 to April 2003 (Yale). Recruitment methods were similar between sites and included advertisements by the Internet, radio, and print media as well as posting of flyers and word-of-mouth referrals. At screening, eligible candidates provided informed consent and signed the consent form approved by the institutional review boards at either the University of Chicago or Yale University. Participants all received comprehensive physical and psychological assessment for study inclusion examination (for details, see [9,11]). Eligibility criteria were: age between 18 and 75 years, cigarette smoker of at least 12 cigarettes daily for a minimum of 1 year, fluency in English, stable residence, and desire to quit smoking. Candidates were excluded if they had a past-year history of a major medical or psychiatric disorder, substance dependence (except nicotine), a lifetime diagnosis of opioid abuse or dependence; use of opioid or psychotropic medications; elevated hepatic transaminase concentrations (>2.5× normal range); or, for women, were nursing or pregnant. The only differences in recruitment for these studies were minimum smoking threshold (12 cigarettes/day Chicago vs. 20 Yale) and targeting of minorities (27) (35% African Americans Chicago vs. 7% Yale).

Procedures

The two studies were similar in general procedures, including a double-blinded design, randomization to naltrexone hydrochloride (Mallinckrodt Pharmaceuticals, St. Louis, Missouri) or placebo, and inclusion of standard smoking cessation treatment platform with open-label transdermal nicotine patch (Nicoderm CQ; GlaxoSmithKline, Brentford, Middlesex, United Kingdom) and behavioral counseling. The main differences between studies involved medication dosing and length of treatment. All naltrexone-randomized participants in the Chicago study received 50 mg as the dose for 12 weeks compared with naltrexone randomization to 25-, 50-, or 100-mg doses for 6 weeks at Yale. Participants in the Chicago study took the nicotine patch at 21 mg daily for the first 2 weeks after the quit date, followed by 14 mg during the third week, and 7 mg during the fourth week, compared with 21 mg daily for the 6 weeks at Yale. Finally, behavioral counseling included six 45-min sessions ending at 4 weeks after the quit date at Chicago compared with a 45-min initial session and then five 15-min sessions ending at 6 weeks at Yale. As with most stop-smoking behavioral counseling treatments, the interventions focused mainly on smoking cessation techniques with the inclusion of a brief module to address potential weight gain.

At the first study visit, which was 1 week before the quit date, height and weight were measured on all participants. Also at baseline, participants were administered a Timeline Followback (28) interview to assess past-month cigarette smoking. At follow-up 6 and 12 months after the quit date, participants completed a telephone-delivered Timeline Followback interview and, if they had a 7-day point prevalence of smoking abstinence, were scheduled for an in-person visit to provide a breath test to assure carbon monoxide ≤10 ppm and have weight measured. For weight measurement, participants at both sites were asked to first remove their shoes and coat, as appropriate. Weight was measured by a calibrated digital (Chicago) or beam scale (Yale). Participants were conservatively classified as relapsed if they did not participate in follow-up or provide biochemical confirmation, and therefore they were not included. Percentage increase in body weight was calculated for each follow-up interval, and BMI was calculated as weight divided by height (in kg/m^2), with baseline height used in all calculations, because height changes over time were assumed to be negligible.

Statistical Analyses

Sociodemographic and background characteristics were compared by sex and group with analysis of variance or logistic regression, as appropriate. The weight change from baseline to 6- and 12-month follow-up in kilograms and percentage change in body weight, BMI change, and clinically significant weight gain of ≥7% of baseline body weight (binary) were analyzed by Generalized Estimating Equation models with an identity link function for continuous measures or a logit link function for binary measures. For each outcome, controlling for study site, two generalized estimating equation models were analyzed: 1) including medication, follow-up time, and their interaction; and 2) including medication, time, sex, and the two-way and three-way interaction among them.

Results

Among the confirmed smoking abstainers, 157 of 159 (99%) had weight recorded at their 6-month follow-up, and as expected, most gained weight: 132 participants (84%) gained between .2 and 12.6 kg, with an average gain of 5.3 (SD = 3.0) kg, 2 participants (1%) experienced no weight change, and 23 participants (15%) lost weight, ranging from .2 to 20.9 kg, with an average loss of 4.0 (SD = 4.8) kg. Two otherwise healthy but overweight or obese male participants from Yale (BMIs of 28 and 30 kg/m^2) at follow-up had lost 12.7 and 20.9 kg, respectively. Because they were statistical outliers (>3 SD) on the basis of the whole sample as well as among the sample subsets of men only or overweight participants only, they were not included in the remaining analyses. After removing them, the average decrease in those who lost weight was 2.7 (SD = 2.5) kg. Among the 115 who remained abstinent at 12 months, 112 (97%) had weight recorded, and the vast majority experienced cumulative weight gain: 98 participants (87%) gained between .2 and 18.7 kg, with an average gain of 6.9 (SD = 4.4) kg; 2 participants (2%) had no weight change; and 12 participants (11%) lost weight, ranging from .2 to 8.4 kg, with an average loss of 2.9 (SD = 2.6) kg.

Table 1 displays the baseline characteristics in the overall sample and for the naltrexone and placebo groups by sex. The groups were similar on most background characteristics with the exception that men were significantly younger and weighed more than women. Neither age nor baseline weight was associated with weight gain at 6 or 12 months (r values ≤ .12), so they were not included as covariates.

Table 2 depicts the mean change in weight (in kilograms or percent) and BMI from baseline to 6- and 12-month follow-up as well as the incidence of gaining ≥7% total body weight. There was a significant effect of time indicating greater weight gain at 12 months compared with 6 months [β(SE) = .45 (.11), $p < .001$], but there was no significant medication effect or interaction between medication and time ($p > .05$) (Table 2). Including sex in the model revealed several significant effects (Table 3), including a medication × sex interaction for weight change in kilograms (Figure 1), percentage body weight, and BMI. Postestimation tests revealed that, in the placebo group, women gained significantly more weight [β(SE) = 2.46 (1.08), $p < .05$] and experienced greater increases in BMI [β(SE) = 1.07 (.39), $p < .01$] and percent body weight [β(SE) = 3.87 (1.38), $p < .01$] than men. Naltrexone also significantly reduced weight gain [β(SE) = −2.10 (.99), $p < .05$] in women as well as the gain in percent body weight [β(SE) = −2.62 (1.26), $p < .05$] and BMI [β(SE) = −.80 (.36), $p < .05$], but this was not the case for men. Examination of the dichotomous index of clinically significant weight gain of ≥7% baseline body weight indicated that naltrexone tended to reduce this incidence in women [β(SE) = −.72 (.42), $p = .087$] but not in men, and in the placebo group, women had a higher incidence than men [β(SE) = 1.29 (.48), $p < .01$] (Table 3).

In addition to the preceding results, which controlled for the main effect of study site, additional analyses were performed to control for the interactions of study site, medication, and sex on weight change over follow-up. Results revealed that none of these interactions was significant [study site × medication: β(SE) = −.51 (2.03), $p = .80$; study site × sex: β(SE) = −2.19 (2.29), $p = .34$; study site × medication × sex: β(SE) = 2.11 (2.88), $p = 0.46$]. Furthermore, analyses examining the effect of tablet and patch adherence during treatment (91% and 88% overall, respectively) on weight change over follow-up showed no associations (−.09 ≥ r values ≤ .05, p values > .21), and including these as covariates did not change the main study findings. Finally, the association between cigarettes/day and weight gain outcomes was examined, and the results showed positive correlations with cigarettes/day, weight, and BMI change at 6 months (r values ≥ .19, p values < .05), indicating that heavy smokers

Table 1. Baseline Characteristics by Treatment Condition and Sex

	Total Sample (n = 155)				By Sex								p		
					Women (n = 77)				Men (n = 78)						
	Placebo (n = 60)		Naltrexone (n = 95)		Placebo (n = 32)		Naltrexone (n = 45)		Placebo (n = 28)		Naltrexone (n = 50)		Med	Sex	Med × Sex
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD			
Age (yrs)	44.9	10.8	45.7	11.8	47.8	9.5	47.9	10.5	41.7	11.4	43.7	12.6	.56	.006	.60
Weight, Baseline (kg)	81.2	16.5	79.9	15.0	76.1	16.7	74.9	15.1	87.0	14.5	84.5	13.6	.45	.0001	.79
BMI, Baseline (kg/m^2)	27.7	4.9	27.4	4.7	27.9	5.1	27.8	5.2	27.4	4.8	27.1	4.2	.79	.47	.89
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%			
Education (≥Some College)	48	80	70	74	24	75	33	73	24	86	37	74	.87	.31	.42
Race (White)	45	75	80	84	23	72	37	82	22	79	43	86	.28	.55	.93
Married/Cohabitating	29	48	50	53	14	44	20	44	15	54	30	60	.95	.45	.73

BMI, body mass index; Med, medication.

Table 2. Weight Change and Related Outcomes in 6- and 12-Month Smoking Abstainers

	6-Month Follow-Up				12-Month Follow-Up						
	Placebo ($n = 60$)		Naltrexone ($n = 95$)		Placebo ($n = 48$)		Naltrexone ($n = 64$)		Med		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	β	SE	*p*
Weight Gain (kg)	4.4	4.3	4.0	3.9	6.2	4.8	5.3	5.5	−1.4	1.6	.38
BMI Increase (kg/m^2)	1.6	1.6	1.4	1.4	2.2	1.7	1.9	2.0	−.3	.3	.32
% Body Weight Gain	5.6	5.4	5.2	5.1	7.7	5.9	7.0	6.9	−.7	.9	.47
	n	%	*n*	%	*n*	%	*n*	%	OR	SE	*p*
≥7% Body Weight Gain	25	42	36	38	26	54	32	50	.8	.3	.52

BMI, body mass index; Med, medication; OR, odds ratio.

might be more vulnerable to postcessation weight gain at this interval. However, there were no associations at 12 months, and including cigarettes/day as a covariate in the main study models did not alter the reported results.

Discussion

The results of this study identify naltrexone as the first pharmacotherapy to reduce long-term smoking cessation weight gain in women. Notably, 6 months after the quit date, which was 3–4 months after tablet discontinuation, naltrexone (vs. placebo) reduced weight gain by approximately 40% in women. At 12 months, naltrexone effects were still evident, albeit somewhat diminished with a 20% reduction in weight gain in women relative to placebo. Naltrexone also reduced other indices beyond raw weight increase that take into account body composition, including BMI increase, percentage increase in body weight, and incidence of clinically significant weight gain in women. Women receiving placebo experienced larger weight gain than men, with an increase of 2.0 kg/m^2 in BMI and more than half (56%) experiencing clinically significant body weight gain at 6 months, with further increases of 2.6 kg/m^2 in BMI and over two thirds (68%) experiencing clinically significant weight gain at 12 months. Increases in weight are known to be associated with numerous medical complications and early mortality (29). Adjunct treatment with naltrexone in the first few months of smoking cessation might be particularly important for women, because they exhibit greater postcessation increases in weight and are more concerned about weight gain (6,30). Although other pharmacotherapies (nicotine replacement, bupropion) have been shown to delay weight gain in those who quit smoking (23), eventual weight gain at follow-up has not differed from those receiving placebo. The most recent 2012 Cochrane Report on interventions to prevent weight gain in smokers (4) indicated that, of all the pharmacotherapies tested, naltrexone showed the most promise, but long-term results were needed. Such data are now reported in this article, with the caveat that reduction of weight gain seems to be evident in women but not men. Because women have more concerns of weight gain when they quit smoking than men, the findings might be highly clinically relevant.

Eating behavior and weight regulation are highly complex and involve numerous neurobiological pathways and processes (21). The opioid system has been shown to be involved in sweet and palatable food intake, eating hedonics, and sugar bingeing (31–33). Targeting μ opioid receptors with the antagonist naltrexone might be a particularly important strategy for women, who are more likely than men to have disordered eating (34) and binge on high-fat and sweet foods (35). As shown in the current study and by others, women are particularly vulnerable to weight gain during smoking cessation (5,36), likely due to enhanced sensitivity to high-fat and high-calorie food reward or related cues during abstinence (37). Nicotine itself produces variable effects on eating behaviors (38), and preclinical studies suggest that, when nicotine is no longer present, food reward enhancement by

Table 3. Weight Change and Related Outcomes in 6- and 12-Month Smoking Abstainers by Sex

	6-Month Follow-Up								12-Month Follow-Up										
	Women ($n = 77$)				Men ($n = 78$)				Women ($n = 57$)				Men ($n = 54$)				Med × Sex		
	Placebo ($n = 32$)		Naltrexone ($n = 45$)		Placebo ($n = 28$)		Naltrexone ($n = 50$)		Placebo ($n = 25$)		Naltrexone ($n = 32$)		Placebo ($n = 22$)		Naltrexone ($n = 32$)				
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	β	SE	*p*
Weight Gain (kg)	5.5	3.9	3.3	4.3	3.1	4.3	4.6	3.4	7.4	5.4	5.9	6.2	5.0	3.7	4.8	4.8	6.79	3.08	.027
BMI Increase (kg/m^2)	2.0	1.5	1.2	1.7	1.0	1.5	1.6	1.1	2.6	2.0	2.2	2.3	1.6	1.1	1.6	1.6	1.13	.50	.023
%Body Weight Gain	7.3	5.4	4.7	5.8	3.7	4.8	5.7	4.3	9.4	6.7	8.0	7.7	5.8	4.2	6.1	6.0	4.09	1.76	.020
	n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	OR	SE	*p*
≥7% Body Weight Gain	18	56	16	36	7	25	20	40	17	68	19	59	9	39	13	41	3.16	1.91	.057

Abbreviations as in Table 2.

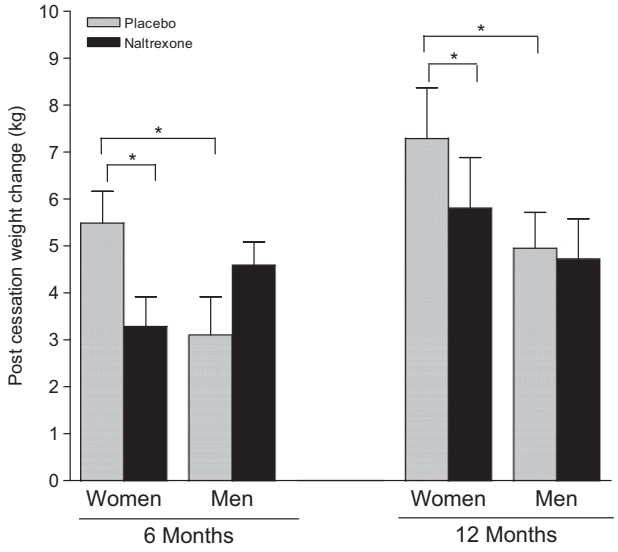

Figure 1. Weight change in 6- and 12-month smoking abstainers. $^{*}p < .05$.

nicotine might persist but satiety might abate, leading to overeating and weight gain. Naltrexone might uniquely alter one of these two mechanisms differently than other medications for tobacco cessation that reduce weight gain initially but not long-term (4). Thus, it is conceivable that naltrexone reduces sex-specific differences in behavioral and neurobiological reward processes and/or stress response pathways (39–42) underlying weight gain in smokers who quit. The study findings complement increasing evidence of patient subgroups most likely to respond to naltrexone in the treatment of alcohol or smoking problems by virtue of genetic factors (43), negative affect (44), sex (8,9), and alcohol/smoking co-use (45–47).

On the population level, weight gain is the most common unintended negative consequence of quitting smoking and might exacerbate the already high overweight and obesity rates in the U.S. (48). As such, health economists extrapolating obesity trends over the past 3 decades have forecasted that the population benefit observed from successful treatment of tobacco dependence will be greatly reduced if prevention or reduction in postcessation weight gain is not addressed (48). In addition, although smokers in general have lower BMI than nonsmokers, they also have greater abdominal fat deposition, larger insulin resistance, and higher rates of metabolic syndrome (49), all of which increase their risk for major medical problems and early mortality. Therefore, a medication that can reduce long-term weight gain is of clinical significance. Because there is a significant increase in risk for death and medical comorbidities due to excessive weight in persons with BMIs ≥25 kg/m^2 (50), and our sample—like most treatment-seeking samples—averaged in the overweight range, any increase in weight and percent body weight might be medically important, besides being personally undesirable.

The current study had several strengths, including combining follow-up data from the two largest clinical trials of naltrexone in smoking cessation and enabling adequate power to examine medication and sex effects and their interaction on weight change of smokers over time. Although prior studies have shown short-term effects of naltrexone in reducing early cessation weight gain over several weeks (8–11), examination of longer-term effects has not been possible, because it requires sample sizes of abstainers during follow-up exceeding even those in the largest individual trials, because only a minority of smokers are able to quit even with the most efficacious treatments (23). Indeed, in the current study, the number of abstinent participants 12 months after the quit date was 16% (115 of 700) of the overall combined intent-to-treat dataset. Also, we reported on weight-gain changes over time (i.e., at 6- and 12-month follow-up), with the advantage of examining naltrexone effects on weight gain over two long-term posttreatment intervals rather than just cross-sectionally at one interval. However, because the combined analysis did include two individual trials, there were some notable differences, such as length of treatment (12 weeks at Chicago vs. 6 weeks at Yale) and choice of naltrexone dose (50 mg at Chicago vs. 25, 50, or 100 mg at Yale). Therefore, this precluded dose analyses, because cell sizes were particularly small for the 25- and 100-mg levels, and conclusions about optimal dosing of naltrexone for reduction of weight gain or optimal length of treatment will not be possible until multi-site dose-ranging studies are conducted. Also, participants were enrolled in clinical trials with exclusion criteria for major psychiatric comorbidities and requirements for numerous visits, measures, and compensation for time and travel, which might not be reflective of standard smoking cessation. However, that the effects of naltrexone in reducing weight gain of women was observed despite the inherent differences between studies highlights that opioid antagonist effects for women might be particularly robust.

In conclusion, naltrexone produced reductions in weight gain in women who quit smoking but not in men. This is the first evidence for a pharmacotherapy to produce long-term reduction in weight gain in abstinent smokers. It is unclear why effects of naltrexone were evident particularly for women, but women exhibited heightened weight gain during cessation compared with men, and it is possible they are more sensitive to opioidergic and dopaminergic processes underlying eating behaviors (21,39), which might be altered by μ opioid antagonism. Unwanted weight gain is the most common consequence of smoking cessation, and it might further exacerbate the myriad of health problems associated with being overweight and obese as well as deter a sizable portion of smokers, particularly women, from trying to quit smoking. Adjunctive treatment with naltrexone to standard smoking-cessation treatment with nicotine patch and counseling might alter dysregulated food intake processes in women during the critical early interval of a quit attempt and reduce the extent of their weight gain post cessation.

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Clinicaltrials.gov: Efficacy of Naltrexone in Women's Smoking Cessation; http://clinicaltrial.gov/ct2/show/NCT00271024?term=NCT00271024&rank=1; NCT00271024.

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