ONDAMED® and Smoking Cessation – A Statistical Analysis

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This report analyzes data from two groups of subjects treated with ONDAMED® for smoking cessation. Group 1 includes *n*=103 subjects while Group 4 includes *n*=74 subjects. Data from Groups 2 and 3 were not suitable for analysis because the period is either unreported (Group 2) or vague (Group 3). The statistical analysis consists of the percentage of subjects within each group who were nonsmokers at each time at which data are reported, along with 95% confidence intervals for the percentages. Each group is analyzed separately and in combination.

In addition, this report compares the results from the ONDAMED® trials with those from Shiffman, et al.[1], who tested the efficacy of nicotine gum in facilitating smoking cessation through gradual reduction. The statistical analysis consists of hypothesis tests to determine if the success rate one month and six months after 24-hour abstinence while using nicotine gum differs from the success rate one month and six months after treatment with ONDAMED®.

Results

Success Rates in ONDAMED® Trials

Table 1 and Figure 1 show the results for Group 1, Table 2 and Figure 2 show the results for Group 4, and Table 3 and Figure 3 show the results for the combined groups.

Table 1: Results for Group 1 (103 subjects). ME = Margin of Error for the 95% confidence interval.

Time	Nonsmokers	Percentage	ME	Lower CI	Upper CI
0 days	103	100.0%	0.0%	100.0%	100.0%
14 days	86	83.5%	7.2%	76.3%	90.7%
1 month	77	74.8%	8.4%	66.4%	83.1%
3 months	65	63.1%	9.3%	53.8%	72.4%
6 months	52	50.5%	9.7%	40.8%	60.1%
1 year	40	38.8%	9.4%	29.4%	48.2%

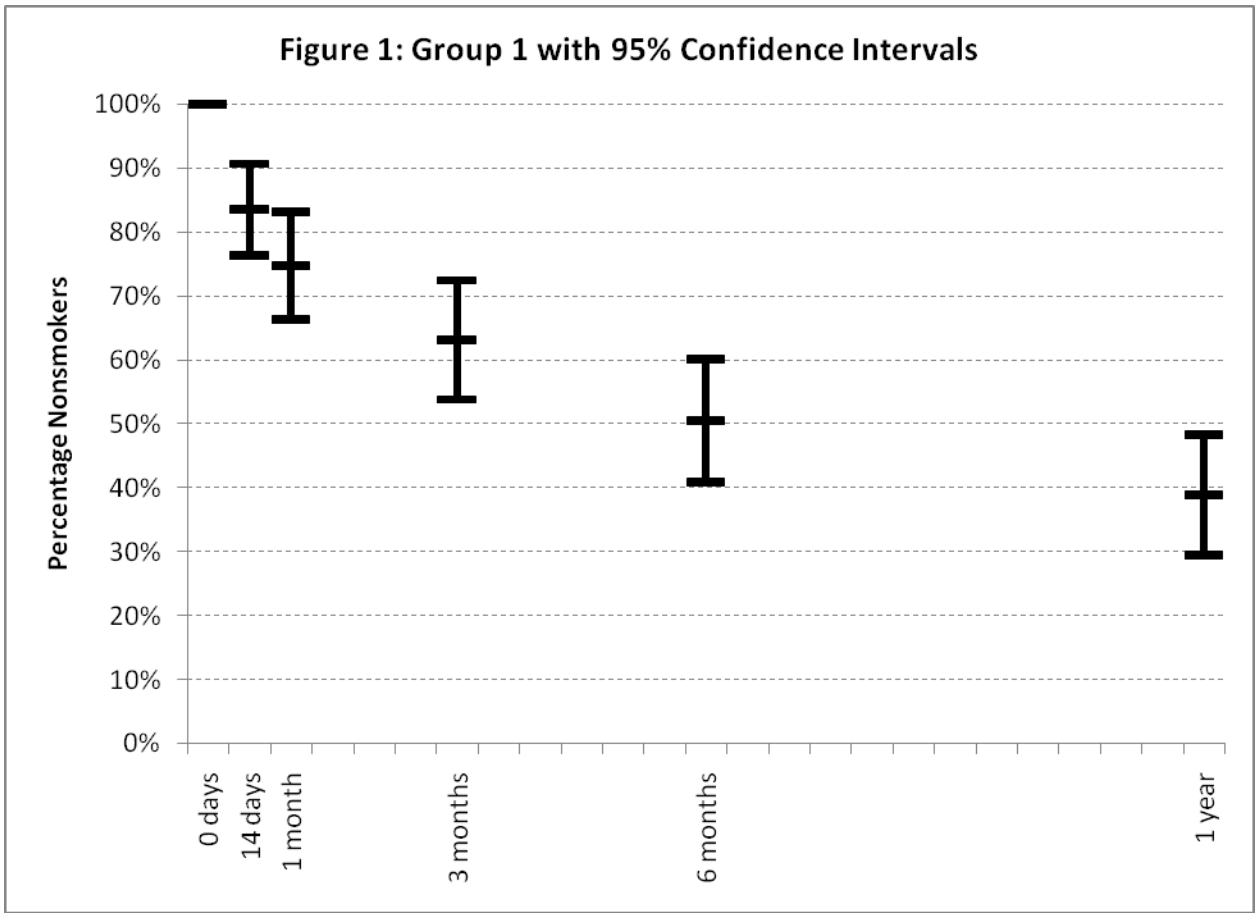


Table 2: Results for Group 4 (74 subjects). ME = Margin of Error for the 95% confidence interval.

Time	Nonsmokers	Percentage	ME	Lower CI	Upper CI
0 days	74	100.0%	0.0%	100.0%	100.0%
14 days					
1 month					
3 months					
6 months	54	73.0%	10.1%	62.9%	83.1%
1 year					

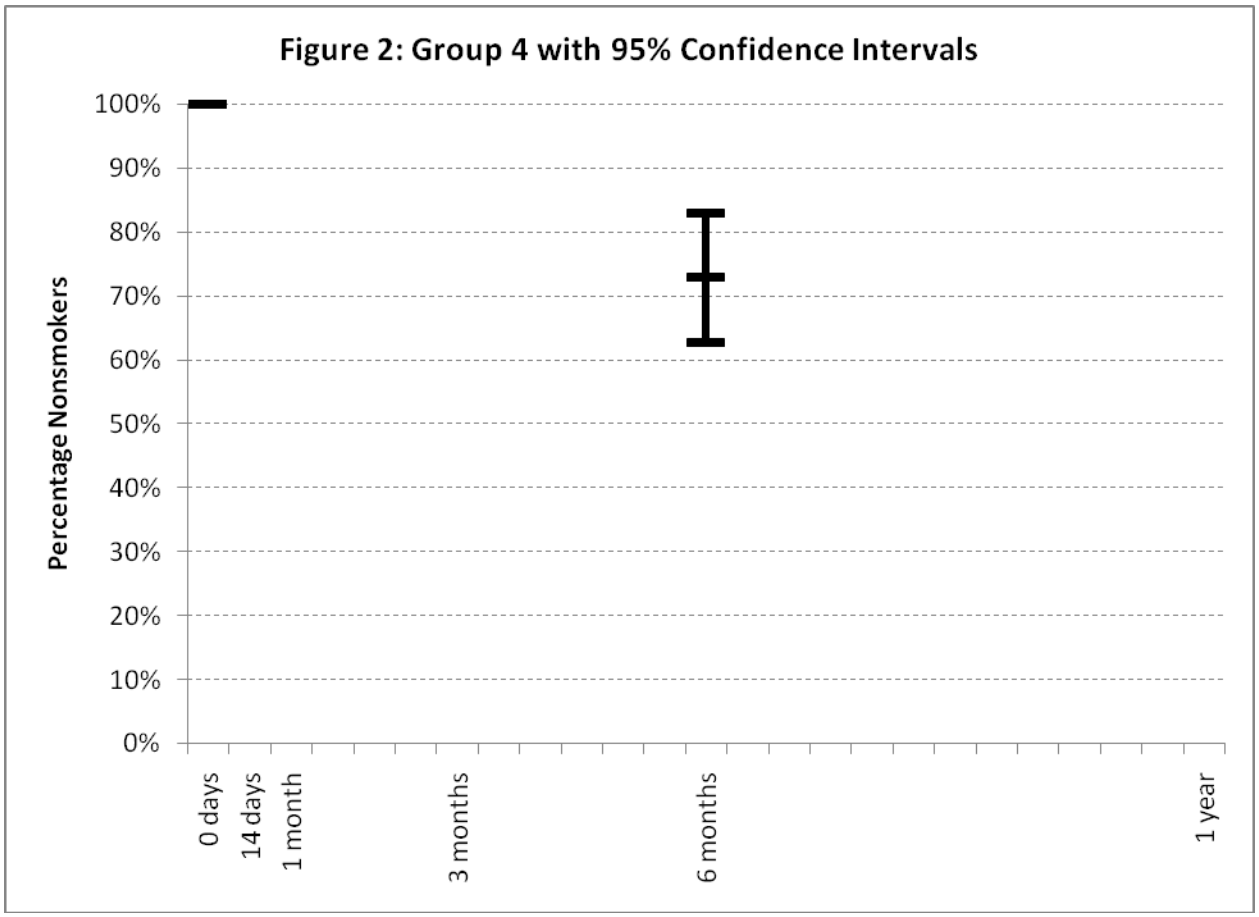
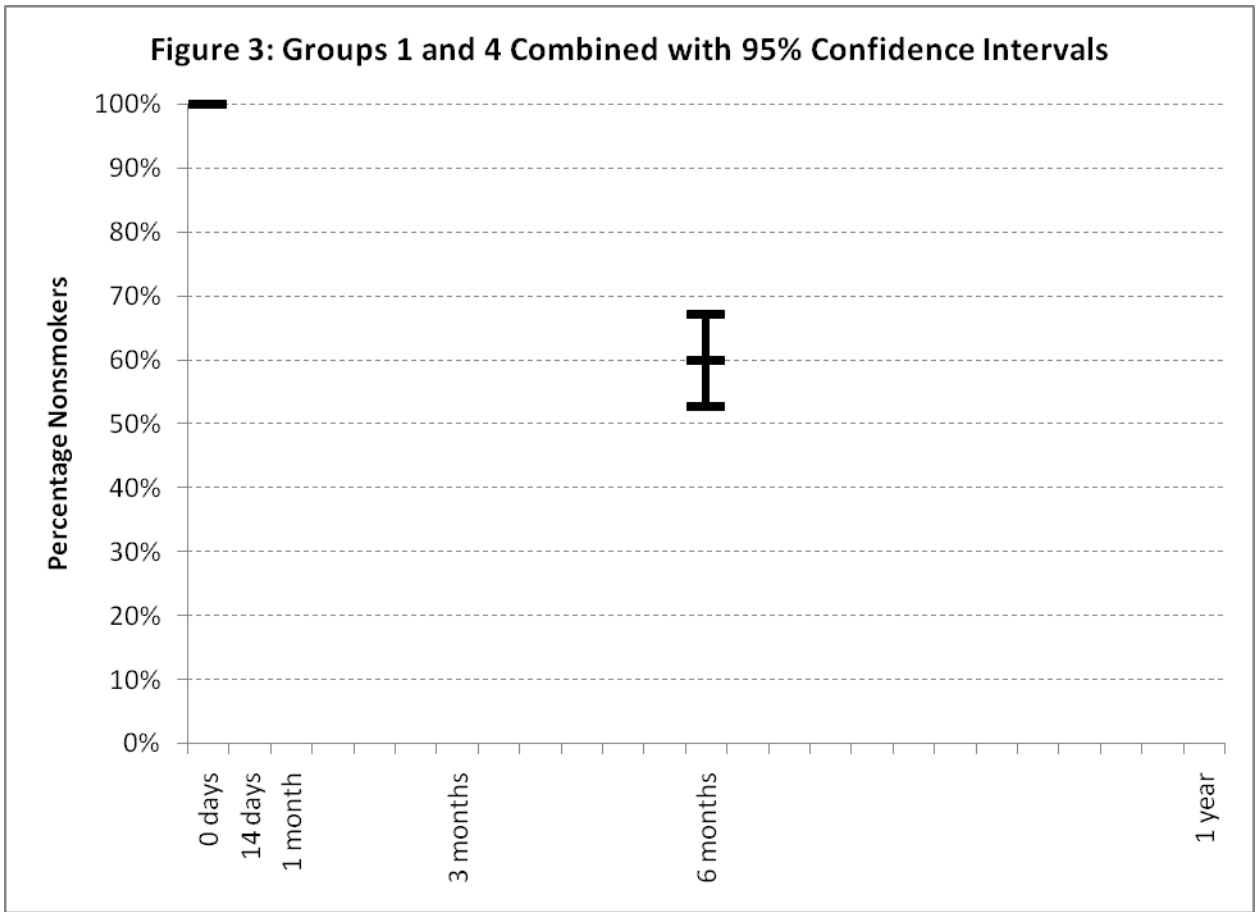


Table 3: Results for Groups 1 and 4 combined (177 subjects). ME = Margin of Error for the 95% confidence interval.

Time	Nonsmokers	Percentage	ME	Lower CI	Upper CI
0 days	177	100.0%	0.0%	100.0%	100.0%
14 days					
1 month					
3 months					
6 months	106	59.9%	7.2%	52.7%	67.1%
1 year					



Comparison of ONDAMED® with Nicotine Gum

Shiffman, et al.[1] enrolled 3297 smokers who then self-selected either 2-mg or 4-mg nicotine gum after reviewing the label instructions, which told subjects who smoked at least 25 cigarettes per day to select the 4-mg dose and those who smoked less to select the 2-mg dose. Self-selection complied with these instructions in 88.3% of all cases, with 1636 subjects in the 2-mg group and 1661 in the 4-mg group. Within each dosage group, subjects were randomly assigned to either treatment with the selected dose or a placebo gum. All subjects were instructed to gradually replace cigarettes with gum for one additional hour per day until they achieved abstinence from smoking for 24 hours. They then continued to use the gum according to FDA-approved labeling for 12 weeks and then "as needed to stay smoke-free" for an additional 12 weeks.

The primary study endpoint was achievement of 28-day continuous abstinence. Reduction in smoking, achievement of initial 24-hour abstinence, and abstinence at six months were also reported. Table 4 shows the progression of subjects through the trial.

Table 4: Progression of subjects through the trials reported in Shiffman, et al.[1]

Enrolled	*n* = 3297			
Self-Selected Group	2-mg; *n* = 1636		4-mg; *n* = 1661	
Randomly Allocated	817 placebo	819 active	831 placebo	830 active
24-Hour Abstinence	195	252	109	184
28-Day Abstinence	45	86	21	88
6-Month Abstinence	40	75	18	78

The success rates using nicotine gum may be computed in two ways. In the first method, we use the number of subjects randomly assigned to active treatment as the denominator. In the second method, we use only those subjects in the active treatment group who achieved 24-hour abstinence as the denominator. Table 5 shows the success rates for ONDAMED® along with the success rates for the 2-mg dose of nicotine gum, while Table 6 shows the results for the 4-mg dose of nicotine gum.

Table 5: Success rates for ONDAMED® and 2-mg nicotine gum at one month (28 days) and six months.

Time	Ondamed®	2-mg Nicotine Gum	
		All Subjects	24-Hour Abstinence
1 Month (28 Days)	77/103 = 74.8%	86/819 = 10.5%	86/252 = 34.1%
6 Months	106/177 = 59.9%	75/819 = 9.2%	75/252 = 29.8%

Table 6: Success rates for ONDAMED® and 4-mg nicotine gum at one month (28 days) and six months.

Time	ONDAMED®	4-mg Nicotine Gum	
		All Subjects	24-Hour Abstinence
1 Month (28 Days)	77/103 = 74.8%	88/830 = 10.6%	88/184 = 47.8%
6 Months	106/177 = 59.9%	78/830 = 9.4%	78/184 = 42.4%

There are eight comparisons of ONDAMED® versus nicotine gum: two dosages at two times and using two denominators (all subjects and only those who achieved 24-hour abstinence). Each comparison involves a two-tailed, two-sample hypothesis test of proportions, which were performed using the normal distribution test with correction for continuity. In all comparisons except one, the P-value for the test is less than 0.00005. In the comparison of ONDAMED® versus 4-mg nicotine gum at 6 months and using only those subjects who achieved 24-hour abstinence, the P-value is 0.0013.

Thus, we conclude with near certainty that the subjects who were treated with ONDAMED® experienced a higher success rate at both one month and six months than did those who used nicotine gum at either dose.

There are at least two caveats that apply to this conclusion.

1. The subjects in the Shiffman, et al., study had all expressed the desire to quit smoking gradually rather than at once. Thus, they may have been less committed to quitting than some of the patients in the ONDAMED® study.
2. The subjects in the Shiffman, et al., study were tested twice for carbon monoxide in their breath and, in some cases, for serum cyothianate to protect against unreliable self-reporting of smoking behavior.

Reference

1. Shiffman S, Ferguson SG, Strahs KR. Quitting by gradual smoking reduction using nicotine gum: a randomized controlled trial. Am J Prev Med 2009;36(2):96-104.