'Cold turkey' or pharmacotherapy: Examination of tobacco cessation methods tried among smokers prior to developing head and neck cancer

Samir S. Khariwala, MD, MS[1,2], **Nathan Rubin, MS**[2,6], **Irina Stepanov, PhD**[2,4], **Nicole Nollen, PhD**[8], **Jasjit S Ahluwalia, MD, MPH**[7], **Heather H Nelson, MPH, PhD**[2,5], and **Dorothy K Hatsukami, PhD**[2,3]

[1.]Department of Otolaryngology-Head and Neck Surgery, University of Minnesota

[2.]Masonic Cancer Center, University of Minnesota

[3.]Department of Psychiatry, University of Minnesota

[4.]Division of Environmental Health Sciences, School of Public Health, University of Minnesota

[5.]Department of Epidemiology and Community Health, University of Minnesota

[6.]Department of Biostatistics, University of Minnesota

[7.]Department of Behavioral and Social Sciences, Brown University School of Public Health

[8.]Department of Preventive Medicine and Public Health, University of Kansas

Abstract

Background: Tobacco cessation methods employed by Head and Neck Cancer (HNSCC) patients are previously unstudied and have the potential to inform choice of cessation method and necessary abstinence support.

Methods: 130 current smokers with HNSCC were queried regarding prior unsuccessful tobacco cessation techniques, product used (cold turkey, varenicline, nicotine patch/gum), and maximum time abstained from smoking.

Results: 106 smokers retrospectively reported using one of the four main quit methods. Unassisted cessation ("cold turkey") was the most commonly used method (p<0.0001). A multiple ordinal logistic GEE analysis revealed that cold turkey had increased odds [5.2 (95% CI: 2.2, 11.8) and 4.3 (95% CI: 1.5, 12.9)] of achieving a longer quit duration than the nicotine patch or varenicline, respectively.

Conclusions: Among smokers developing HNSCC, previous cessation attempts were most commonly unassisted. This method was associated with longest abstinence periods. These data suggest insufficient support and education regarding behavioral and pharmacologic cessation therapies.

Corresponding Author: Samir S. Khariwala, MD MS, Dept of Otolaryngology-Head and Neck Surgery, University of Minnesota, MMC 396, 420 Delaware St SE, Minneapolis, MN, 55455, khari001@umn.edu, 612-626—0912, Fax: 612-625-201.
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Keywords

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Background

Head and neck squamous cell carcinoma (HNSCC) is a disease most frequently related to past or current tobacco use. While human papillomavirus (HPV) has recently been identified as a frequent cause of oropharyngeal cancers, most head and neck cancers in the oral cavity, larynx, hypopharynx (any many in the oropharynx) are associated with tobacco use[1]. As the national emphasis on disease prevention grows, a greater focus on tobacco cessation is warranted as a means to discontinue exposures to carcinogens, thus reducing the risk of HNSCC. While the treatment options for those seeking smoking cessation have grown to include nicotine replacement and pharmacotherapies, it continues to be an unfortunate truth that most who attempt to quit smoking are ultimately unsuccessful. Approximately 2/3 of all US adult smokers surveyed in 2013 reported attempting to quit in the past year but the rate of successful, durable cessation is 3–5% at one year [2–5] in the general population.

Presently, smokers wishing to quit have pharmacologic treatments available to them that have been shown to increase their chances of quitting. In the US and Europe, approved treatments for smoking cessation include nicotine replacement therapy (NRT), sustained-release (SR) bupropion and varenicline (Chantix). The latter acts through binding of nicotinic acetylcholine receptors and is a partial agonist, with both agonist and antagonist effects. NRT and SR bupropion (which increases the same neurochemical increased by nicotine) have been found to approximately double (OR for bupropion: 1.94) the chances of successful abstinence at 6 to 12 months compared to unassisted attempts [6, 7]. Abstinence rates at 12 months in the general population for NRT and bupropion range from 10–31%[8, 9] and 23–30% [10, 11], respectively. Varenicline also improves the abstinence rates when compared to placebo by 2.5 to 3 times (Varenicline: 44% vs Placebo: 18%) at 12 months [12, 13].

Despite availability of pharmacologic therapy for tobacco cessation, there is scant literature regarding the use of these therapies among smokers developing HNSCC. While there is ample evidence that smoking cessation at diagnosis or prior to the start of therapy is an important part of optimizing disease control [14], we know very little about the most frequently used smoking cessation approaches and products in this population. There is, however, evidence that a significant portion of patients diagnosed with HNSCC continue to smoke after surgical therapy [15]. Still, additional data suggest that a systematic approach aimed at encouraging cessation coupled with intensification for those who are less able to quit can improve overall abstinence rates in HNSCC patients [16]. Our recent study showed that most smokers with HNSCC have made multiple prior cessation attempts (Khariwala et al, *In Press*) such that there may be an opportunity to incorporate newer cessation treatments into systematic programs to achieve smoking cessation at the time of diagnosis with HNSCC. Efforts of this type would be aided by better understanding of patients' prior experience with cessation methods and their respective success rates. The primary objective

of the current retrospective report is to compare the rates of use for multiple tobacco cessation therapies in smokers who have gone on to develop HNSCC while also investigating the relative success rates for each product.

Materials and Methods

Study subjects:

This retrospective, cross-sectional study was approved by the University of Minnesota Research Subjects' Protection Programs Institutional Review Board: Human Subjects Committee (IRB Study # 0903M62203). HNSCC patients were identified at clinic visits to the Otolaryngology-Head and Neck Surgery clinic with a new diagnosis of squamous cell carcinoma of the upper aerodigestive tract. This included tumors of the oral cavity, oropharynx, larynx and hypopharynx. In some cases, cancers were first identified in our clinic, whereas in others, cancers were diagnosed at outside institutions and referred to our clinic for definitive management. Inclusion criteria included self-report of current daily smoking and having smoked at least 5 cigarettes per day for at least 5 years. A total of 130 smokers were eligible and enrolled in the study from February 2009 to October 2017. Patterns of tobacco cessation attempts and symptoms experienced in this sample have been recently described[17].

Questionnaire:

All subjects completed questionnaires regarding their lifetime tobacco and alcohol use. The questionnaire is based on the Tobacco Use History Questionnaire [18]. Data collected include cigarettes per day, duration of use, alcoholic drinks per day, and other drug related behaviors.. In addition, subjects answered questions regarding cessation assistance methods used during prior abstinence attempts and length of quit periods. Prior quit attempts outside of our clinic were queried via checklist (cold turkey, nicotine patch, nicotine gum, nicotine nasal spray, nicotine inhaler, Bupropion (Zyban), clonidine patches, hypnosis, acupuncture, stop smoking clinic, nicotine lozenge, Varenicline (Chantix) and smokeless tobacco/chew) as well as their longest period of using each method and longest period of abstinence. The latter two answers were written in by the subjects. The use of cessation techniques including "cold turkey", nicotine replacement therapies, varenicline, bupropion, hypnosis, acupuncture and smokeless products were queried. However, due to infrequent use of many techniques, analysis was restricted to "cold turkey", nicotine gum/patch, and varenicline. While clinical data (i.e. tumor stage and subsite) was extracted from the medical record, tobacco use and cessation data was gathered via self-report as most subjects were visiting our institution for the first time such that no prior cessation data existed. In addition, the medical charting systems commonly in use are not well optimized to capture tobacco cessation method data. All data was stored on a secure server at the University of Minnesota.

Statistical methods:

Summary measures were calculated for the demographic variables and the two outcome variables (# of times tried and longest smoke-free duration) by method used. Frequencies were calculated to show which of the four primary methods (cold turkey, nicotine patch, nicotine gum, and varenicline) were used at least once in the subject's life. Chi-square

goodness of fit and Tukey's HSD post hoc test were used to explore the differences in the patterns of methods used. To account for the within-subject correlated nature of thesedata (subjects often used more than one method during their life), ordinal logistic general estimating equation (GEE) models were used to model the longest smoke-free duration by method. A multiple ordinal logistic GEE model was also used to model the effects of method on smoke-free duration, while controlling for the number of attempts per method, pack years, and gender. These covariates were selected a priori to capture smoking behavior and intensity, as well as due to the relative completeness of these data. In order to improve the modelling by reducing the impact of outliers and recall bias, the longest smoke-free variable was converted into 5 ordinal categories (0 days, 1 – 7, 8 – 30, 31 – 180, and greater than 180 days).

Results

Demographics:

484 potential subjects were approach for enrollment, 103 declined enrollment, and 168 were found ineligible. An additional 75 subjects were not enrolled for other reasons (i.e. subject was eligible and interested but did not have time to complete enrollment), and 1 subject withdrew. Seven subjects did not have sufficiently completed questionnaires for this analysis. Thus, 130 subjects (smokers with HNSCC) were analyzed in this study. 106 out of the 130 smokers reported using any of the four main quit methods in this study (cold turkey, varenicline, nicotine patch/gum). However, 100 and 89 of these subjects had non-missing data for overall quit attempts and longest smoke-free duration across the four primary methods, respectively (Table 1). Demographic data is summarized in Table 1. The median age of enrolled subjects was 58 years, 80% were male, and 20% were female. Patients presented with squamous cell cancers of oral cavity (26%), oropharynx (34%), larynx (27%) and hypopharynx (8%). The median current cigarettes smoked per day was 15 (IQR 9.75, 20), the median duration of smoking "fairly regularly" was 40 years (IQR 35, 47). Of the 82% of subjects who attempted to quit with at least one of the four primary methods, a median of 4.5 lifetime smoking cessation attempts across the four main methods was reported.

Cessation method use:

When examining the smoking cessation method used in this sample and their relative success, "cold turkey" represents the technique used most frequently. Of those who had used any of the four primary methods (n=106), 86 (81%) used cold turkey (without use of pharmacological agents or behavioral treatments) as one of their methods, while 62 (59%) used the nicotine patch, 32 (30%) used varenicline, and 29 (27%) used nicotine gum as one of their methods (chi-square: p<0.0001). These data are displayed in Table 2; the percentages sum to greater than 100% because many subjects used more than one method during their lifetime. During questionnaire completion, all subjects confirmed using one method at a time as opposed to using combinations of several methods concurrently. Table 3 addresses the use of multiple methods (at different times of their life) for cessation. Of those subjects using two or more methods during their lifetime, cold turkey was part of the most commonly used combination of techniques in each case. With respect to methods used at

different times over the smokers' lifetime, 31% used cold turkey only, 18% used cold turkey and the nicotine patch, 9.4% used cold turkey, varenicline and the nicotine patch and 10.4% use all four primary methods at different times (Table 3).

Subjects were most likely to use only one method in their lifetime (40.6%), followed by 2 (32.1%), 3 (17.0%) and 4 (10.4%) methods (Table 3, Chi-square, $p < 0.0001$). Furthermore, those who used cold turkey were less likely to try other methods at another time compared to those who used varenicline, nicotine gum or the nicotine patch. Those who used cold turkey used on average 1.1 additional methods, which was significantly less than the other three methods, according to Tukey's HSD pairwise test (Table 2). Many of the subjects examined used multiple methods for tobacco cessation over their lifetime. However, of those that used only one method (N=43), cold turkey was used at a rate approximately five times greater than the nicotine patch. Of those who used two methods during their lifetime (N=34), the combination of cold turkey and the nicotine patch was most common (Table 3).

Measures of success:

When considering the number of attempts (Table 4), subjects used the cold turkey method a median of three times compared to the other methods which had median values of one attempt. Cold turkey was also the method associated with the greatest measure of success in the group. Cold turkey resulted in a median cessation length of 60 days, followed by nicotine gum, nicotine patch, and varenicline (5 days, 3.5 days and 1 day, respectively). To account for the within-subject correlation, multiple ordinal logistic GEE with adjustment for covariates of gender, pack years and number of attempts revealed that cold turkey had 5.2 (95% CI: 2.3, 11.8) and 4.3 (95% CI: 1.5, 12.9) and 4.3 (95% CI: 1.8, 10.7) times the odds of achieving a higher quit time than the nicotine patch, varenicline, or nicotine gum, respectively. These were all significant at the level of 0.01. Gender, pack years, and number of attempts were not statistically significant. The rest of the comparisons, as well as the unadjusted model results, are shown in Table 5. There were 76 subjects with complete covariate and response data in the adjusted GEE model, whereas there were 89 in the unadjusted model, which produced very similar results to the adjusted analysis.

Discussion

The availability, and the corresponding use, of smoking cessation assistance has increased over the last 20–30 years[19]. In examining the most frequently used methods of tobacco cessation in a group of smokers diagnosed with HNSCC, we have identified some interesting patterns. Perhaps most significantly, despite the availability of nicotine replacement and other pharmacotherapy (i.e. bupropion and varenicline), unassisted quitting with the "cold turkey" method was the most commonly used cessation method in this group prior to diagnosis. Given that all of the subjects in the study were smoking at the time of enrollment, they (by definition) failed their attempts at cessation regardless of method chosen. Although we do not a have a study group of successful quitters for purposes of comparison, it is nevertheless significant that cold turkey was chosen most frequently both in those who only used one lifetime method, as well as those who used more than one. Furthermore, the metric in this report of longest smoking-free periods again demonstrated

that cold turkey resulted in the greatest success compared to the nicotine patch, nicotine gum and varenicline. Most notably, the median number of days that subjects remained smoke-free after quitting cold turkey was 60 compared to only five days for nicotine gum, 3.5 days for the nicotine patch, and 1 for varenicline. In our sample, most patients made attempts to quit and most frequently did so without assistance despite the availability of pharmacotherapies and other mechanisms of support. Examples of the latter available in the community, but not specifically queried in our questionnaire, include diverse means such as behavioral therapy, telephone quit lines and even an NCI-supported "QuitPal" smartphone application that provides support through a mobile device. It is interesting to find that although our subjects should have had access to multiple assistance measures, they overwhelmingly used cold turkey as their method for cessation. The rate of cold turkey users seen in our study was higher than that previously reported in the general population (approximately 60%[20]) but literature is lacking in those who have cancers at other subsites. This may be due to a perception among smokers developing HNSCC that pharmacologic methods are expensive or related to lack of education regarding how to use the medications and their side effect profiles. Additionally, smokers may (in many cases accurately) perceive that pharmacologic therapies are frequently unsuccessful and decide that the limited benefit is not worth the cost of the therapy. On the other hand, this result may be due to poor clinician engagement in 1) offering smoking cessation advice, 2) giving strong recommendations to use pharmacotherapies or 3) assistance to obtain access to pharmacotherapy. Regardless, the poor uptake of assisted cessation is problematic at a population level in that there is great health-related and financial cost associated with underuse. As a society, striving to embrace all methods of tobacco cessation is likely to reduce tobacco-related morbidity.

With the introduction of nicotine replacement therapies, bupropion SR and varenicline, smokers have many more options for assistance with tobacco cessation. Given the highly addictive properties of cigarettes, these therapies have generally been welcomed as much needed assistance to overcome the physical and psychological dependence that occurs in smokers. The growth of pharmacotherapies for smoking abstinence and rising prominence of anti-tobacco campaigns likely explains the trend of steadily increasing use of assisted abstinence [19]. While the cold turkey method of abrupt cessation is perhaps the oldest method, it continues to be popular among smokers wishing to quit despite relatively low rates of success[21]. Unfortunately, there has been a general dearth of research on unassisted tobacco cessation. Chapman et al contend that public health officials and primary care providers should not immediately discount the value of unassisted attempts at abstinence as that leads to a stigma in which smokers believe assisted cessation is the only way to be successful [22]. In reality, Chapman argues, unassisted cessation is the most common method used (as seen in our data as well) and is often successful. Thus, Chapman suggests providers should exercise caution in "megaphoning" the message that any serious attempt at abstinence requires pharmacotherapy. This results in less research and publicity focused on unassisted cessation while ignoring data that indicate cessation is either "not difficult at all" or "fairly difficult" in 53% and 27% of smokers, respectively, according to a study by Marsh[23]. The general consensus, however, is that clinicians should encourage the use of medications and/or behavioral therapy for tobacco dependence, when not medically contraindicated, given the high cost-effectiveness compared to the alternative of medical

interventions to address sequelae of long-term tobacco use[24]. Behavioral therapy, discussed in more detail below, has been found to be effective but is unfortunately under-utilized by clinicians most likely due to lack of provider education and awareness[25, 26]. Ultimately, successful abstinence is critical among patients diagnosed with cancer because of smoking's effects on treatment outcome and possibly survival [14].

Varenicline is one of the most effective tools for smoking cessation. A randomized trial comparing the use of varenicline, bupropion SR and placebo showed that varenicline was associated with higher rates of abstinence [11]. Varenicline resulted in 23% long term abstinence compared to 15% for bupropion SR and 10% for placebo. The improvement in abstinence with varenicline was confirmed in a third study [27]. Thus, given the well documented effects of varenicline as described in the literature, the finding that varenicline led to a median quit time of only 1 day in our study is in contrast to what would be expected. One possible explanation for this is adverse reactions resulting in decreased use of the medication. In a prior study, ten percent of those taking varenicline had to cease use due to adverse effects and 30% reported nausea from the medication. Another study comparing varenicline to placebo again showed its effectiveness: 23% of those on varenicline achieved long-term (12 months or greater) abstinence vs 4% for placebo but 16–42% reported nausea from the medication [28]. Although our study was not designed to query the reasons behind choice of cessation method, we hypothesize that some choices (i.e. to not use varenicline) in this sample may have been driven by economic considerations in addition to the concerns about adverse reactions, education and clinician engagement described above. In general, head and neck cancer patients occupy a lower socioeconomic status. Thus, the cold turkey method may hold appeal among HNSCC patients based on financial concerns. Finally, the findings associated with Varenicline success in our sample may be the result of our sampling in which only those who continued to smoke (i.e. smokers who had failed prior cessation attempts) were enrolled.

We found it somewhat surprising that nicotine replacement therapies were infrequently adopted in our study group. These products have also been studied fairly extensively and have shown clear benefit in the achievement of abstinence. A Cochrane review of 150 trials found that NRT use increases quit rates from 50–70% and the efficacy is generally not dependent on additional (i.e, cognitive/behavioral) support[29]. A meta-analysis examining seven placebo controlled randomized trials found that NRT was modestly effective in improving cessation when compared to placebo[30]. Nearly 7% of the NRT users attained abstinence of 6 months, which was double the rate seen in those receiving placebo. Still, these rates of sustained abstinence are relatively low and are somewhat in line with our results in that the subjects we studied did not report high rates of success with NRT. Also notable is that the results regarding NRT obtained in the meta-analysis were from studies which often included regular behavioral "support and monitoring" without which the NRT efficacy may have been even lower. Additional existing literature suggests that the combination of NRT deliveries offers additional efficacy. Piper et al demonstrated that the nicotine patch plus lozenge resulted in significantly higher rates of abstinence (OR 2.34) compared to placebo in a 6 month assessment [31]. Given all of these data, it seems to be safe conclusion that NRT has very modest success when used alone in various populations of

smokers and may be offered in combination therapy or with behavioral support to optimize chances for abstinence.

The main limitation of our study relates to the self-reporting of data. It is well-established that self-report may be subject to error due to memory lapse or, in the case of smokers with a cancer diagnosis, shame or embarrassment may lead smokers to report inaccurately. Because of this, we did not query specifics about prior medication use (i.e. duration/frequency) because requests for such specific information (regarding events that occurred several years ago in many cases) would likely be unreliable. As a result, we cannot be sure that those who used pharmacotherapy for cessation actually used the medications correctly. Still, most of the data regarding questionnaire falsification that is presumably due to shame relates to questions of how much and/or how long one smoked[32]. In contrast, our study was focused on questions pertaining to past attempts at cessation and the methods used. While inaccurate self-report is still possible in our study, we submit that it may be less pervasive in a study of this type. Another limitation relates small samples sizes in our subgroups which may limit generalizability until these data can be confirmed in larger samples and/or additional head/neck cancer clinics. There wawere missing data among the various demographic factors (table 1) that resulted from patients not completing all items on the survey. This potentially impacts the adjusted GEE model, where gender, pack years, and number of quit attempts were used. However, a model was run without the additional covariates and it produced very similar results (Table 5), suggesting that the missing data among the covariates did not appreciably impact our analysis. We did not specifically query subjects about the potential use of some behavioral interventions such as individual or group interventions, app-based therapies, telephone quit lines, etc., but these techniques are likely used very infrequently by our study population. Additionally, we do not know whether severity of dependence was a moderating factor associated with longer duration of abstinence among those who chose to quit unassisted. It is possible that those who made an unassisted quit attempt were less dependent than those who sought medications, which might have contributed to the longer duration of abstinence. This also may be a case of so-called "reverse survivorship bias", where it could be that those who used pharmacotherapies were actually more likely to successfully quit smoking, and therefore be absent from our sample. In future work we would seek to address this by examining HNSCC patients who successfully quit smoking to compare to our sample. Still, our sample of HNSCC patients who are actively smoking at the time of diagnosis is designed to most closely approximate what clinicians most frequently encounter in the clinic.

In summary, we have studied a group of smokers with HNSCC to understand their approaches to tobacco cessation over a lifetime of smoking. We found that unassisted cessation with "cold turkey" attempts was the most commonly used method compared to varenicline, the nicotine patch or nicotine gum. In addition, those who used multiple methods over their lifetime most frequently included cold turkey as a technique. Lastly, while all of our subjects were smoking at the time of enrollment, cold turkey-related cessation attempts were associated with the longest abstinence periods over their lifetimes. These data suggest that smokers developing HNSCC may require more education and counseling with strong engagement from health care providers to heighten the use of assistive measures, including (but not limited to) pharmacotherapy and behavioral therapy/

counseling, that have proven to be more effective in achieving durable abstinence rates. With regard to future directions for this work, we hope to perform similar work in subjects with tobacco-induced cancers occurring in other subsites (i.e. lung, esophagus) to understand the differences in patterns of both tobacco use and cessation by disease site. In addition, we aim to better understand the role played by socioeconomic factors in the choice of methods for smoking cessation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1:

Demographic and response variable summary for all subjects in the sample (n=130). Overall quit attempts represents the total number of quit attempts across all four methods for each subject. Longest smoke-free duration represents the largest number of days abstinent for each subject, using any of the four quit methods. Duration is the patient reported total years of lifetime smoking.

Variable	N non-missing responses	Median (IQR) or N (%)	Min, Max
Age	107	58.0 [54.4, 66]	30, 77
Sex (% M, %F, %missing response)	127	102 (78.5%), 25 (19.2%), 3 (2.3%)	-
Overall Quit Attempts (for all 4 main methods)	100	4.5 [3, 6]	0, 100
Longest Smoke-Free Duration (in days, among any of the 4 methods)	89	60 [7, 240]	0, 7300
Cigarettes per day (CPD)	128	15 [9.75, 20]	0, 45
Duration (years)	106	40 [35, 47]	5, 59
Pack Years	104	29.3 [15.2, 47.1]	0, 88.5
Tumor Stage			
I		16 (12.3%)	
II		13 (10.0%)	
III		18 (13.8%)	
IVa		66 (50.8%)	
IVb		3 (2.3%)	
Missing		14 (10.8%)	
Tumor Site			
Hypopharynx		10 (7.7%)	
Larynx		35 (26.9%)	
Oral Cavity		34 (26.2%)	
Oropharynx		44 (33.8%)	
Missing		7 (5.4%)	

Table 2:

Number and Percentage of subjects using any of the four queried tobacco cessation methods with longest smoke free duration and number of cessation attempts. The % of patients column represents what % used that method out of the number of patients who used at least one of the 4 methods.

Used any of the following methods (Lifetime)			
Method	# of Subjects	% of patients who made at least 1 quit attempt using the method	Mean # of additional methods used
Varenicline	32	30.2%	2.0
Cold Turkey	86	81.1%	1.1
Gum	29	27.4%	2.0
Patch	62	58.5%	1.5
Total (any of the 4 methods)	106	100%	1.6

Table 3:

Number of various tobacco cessation methods used (not the number of attempts) by subjects over their lifetime. Data are from the 106 subjects who used at least one of the four methods.

# of Lifetime Methods Used	Lifetime Methods used	# of Subjects	% of Subjects
1	Cold Turkey	33	31.1%
1	Varenicline	2	1.9%
1	Gum	1	0.9%
1	Patch	7	6.6%
2	Cold Turkey, Patch	19	17.9%
2	Gum, Patch	5	4.7%
2	Varenicline, Cold Turkey	3	2.8%
2	Cold Turkey, Gum	3	2.8%
2	Varenicline, Gum	1	0.9%
2	Varenicline, Patch	3	2.8%
3	Varenicline, Cold Turkey, Patch	10	9.4%
3	Varenicline, Gum, Patch	1	0.9%
3	Cold Turkey, Gum, Patch	6	5.7%
3	Varenicline, Cold Turkey, Gum	1	0.9%
4	Varenicline, Cold Turkey, Gum, Patch	11	10.4%
	Total # patients	106	100%

Table 4:

Descriptive statistics for the longest number of abstinent days and number of attempts made based on those who used a given tobacco cessation method. Data are from the 106 subjects who used at least one of the four methods. The total longest smoke-free represents the longest smoke-free value out of any of the four methods for each subject. The total number of attempts represents the total number of quit attempts across all four methods for each subject.

Longest Smoke-free (days)	N	Mean (SD)	Median (25th, 75th)	Min, Max
Varenicline	24	73.8 (147)	1 [0, 23]	0, 450
Cold Turkey	72	882.1 (2132)	60 [7, 316]	0, 7300
Nicotine Gum	20	29.4 (47.5)	5 [0, 30]	0, 150
Nicotine Patch	45	39.2 (84.2)	3.5 [0, 30]	0, 365
Total (any of the 4 methods)	89	741 (1938)	60 [7, 240]	0, 7300
Number of Attempts				
Varenicline	20	1.4 (0.7)	1 [1, 2]	1, 3
Cold Turkey	53	4.4 (7.0)	3 [1, 4]	1, 50
Nicotine Gum	19	1.6 (2.1)	1 [1, 1]	1, 10
Nicotine Patch	45	4.0 (13.2)	1 [1, 3]	1, 90
Total (any of the 4 methods)	100	6.9 (9.2)	4.5 [3, 6]	1, 100

Table 5:

Ordinal logistic GEE table of Odds Ratios for longest smoke free duration, 95% confidence intervals, and p-values for the pairwise method comparisons in the unadjusted and adjusted models. Quit method was the only covariate in the unadjusted model. Covariates in the adjusted model include quit method, number of quit attempts, pack years, and gender (all not statistically significant). There were 89 subjects with longest smoke free duration data in the unadjusted analysis and 76 subjects in the adjusted analysis.

Parameter	Odds Ratio and 95% CI (Unadjusted)	Odds Ratio and 95% CI (Adjusted)	p-value (Unadjusted)	p-value (Adjusted)
Varenicline (vs patch)	1.18 (0.65, 2.12)	1.19 (0.57, 2.48)	0.589	0.647
Cold Turkey (vs patch)	5.88 (3.08, 11.20)	5.15 (2.25, 11.82)	<0.001	<0.001
Gum (vs patch)	1.37 (0.84, 2.23)	1.19 (0.67, 2.12)	0.212	0.554
Cold turkey (vs Varenicline)	5.00 (2.21, 11.31)	4.34 (1.46, 12.89)	<0.001	0.008
Varenicline (vs nic gum)	0.86 (0.46, 1.62)	1.00 (0.42, 2.39)	0.641	0.996
Cold Turkey (vs Gum)	4.30 (2.08, 8.92)	4.33 (1.75, 10.71)	<0.001	0.002