

# Long-term Smoking Cessation of Preoperative Cessation Programs: A Mini-Review

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## ABSTRACT

Smoking increases the perioperative risks of surgery and millions of smokers undergo major operations each year. Few studies in the literature related to preoperative smoking cessation programs have data regarding long-term rates of abstinence. This article reviews the long-term ( $\geq 12$  months) quit rates of preoperative smoking cessation programs.

**Keywords:** Long-term outcomes; Smoking cessation; Perioperative; Preoperative; Surgery

## INTRODUCTION

Smoking remains a significant worldwide public health issue. Over 8 million people die each year from the effects of tobacco. Approximately 7 million of these deaths are from direct tobacco use and an estimated 1.2 million occur in non-smokers being exposed to second-hand smoke [1]. An estimated 60 million smokers worldwide undergo major surgical procedures each year and it is well known that smoking increases the risks of perioperative complications in this population [2]. While one of the first reports of pulmonary complications after surgery related to smoking was published in 1944 [3], the first randomized trial related to preoperative smoking cessation and its effects on postoperative complications wasn't published until 2002 [4]. Several additional randomized trials evaluating short-term smoking cessation outcomes were published over the next decade, a few of which included perioperative and long-term outcomes up to 12 months after surgery [5]. When compiled, these initial studies suggested improved rates of cessation at 12 months after surgery with intensive smoking cessation programs that lasted 4-8 weeks preoperatively. It has been proposed that surgical patients who are current smokers may benefit the most from intensive preoperative smoking cessation interventions including counseling and nicotine replacement therapy [6]. The perioperative period has been noted to be a "teachable moment" for patients when they are more likely to quit [7-20]. Consequently, this period is ripe for success. While numerous studies focus on short-term quit rates in the perioperative period, this article reviews the long-term ( $\geq$

12 months) rates of smoking cessation of preoperative smoking cessation programs (Table 1).

**Table 1:** Lists the characteristics of studies with at least 12 months of follow-up included in this review.

Characteristics of Included Studies				
First Author (year)	Design	Sample Size and Population	Post-operative Follow-up	% Cessation (control vs. intervention)
Aldrete (1987) [8]	Cohort	N=25; single private hospital; United States	12 months	11.1 vs. 56.3*
Ratner (2004) [10]	RCT	N=237; single academic hospital; Canada	12 months	19.7 vs. 19.8
Villebro (2008) [12]	RCT	N=120; multiple academic hospitals; Denmark	12 months	3.3 vs. 21.7*
Sadr Azodi (2009) [13]	RCT	N=117; multiple academic hospitals; Sweden	12 months	14.5 vs. 32.7*
Thomsen (2010) [14]	RCT	N=130; multiple academic hospitals; Denmark	12 months	9 vs. 13
Lee (2015) [15]	RCT	N=168; single academic hospital; Canada	12 months	8.3 vs. 25.4*
Wong (2012) [19]	RCT	N=286; multiple academic hospitals; Canada	12 months	25.2 vs. 36.4*
Wong (2017) [20]	RCT	N=296; multiple academic hospitals; Canada	12 months	26.2 vs. 42.4*

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Fay (2020) [30]	Retrospective cohort	N=82; single academic hospital; United States	12 months	42.6 <sup>a</sup>
Phillips (2020) [31]	Retrospective cohort	N=82; single academic hospital; United States	24 months	51.7 <sup>a</sup>
Balmer (2020) [32]	Prospective cohort	N=27; single academic hospital; United States	~ 40 months <sup>b</sup>	47.6
Van Slyke (2017) [33]	Retrospective cohort	N=85; single academic hospital; Canada	>21 months <sup>c</sup>	23.8 <sup>a</sup>
Taylor (2017) [34]	Prospective cohort	N=50; single academic hospital; Australia	12 months	28.0 <sup>a</sup>
*p<0.05, (a) No control group, (b) Average time from surgery to completion of survey reported as 3.7 years, (c) Range of follow-up 21 to 159 months. RCT: Randomized Controlled Trial.				

## COUNSELING AND NICOTINE REPLACEMENT THERAPY

One of the first studies to suggest the long-term efficacy of preoperative cessation efforts was published in 1987 [8]. This was a small, single institution study of 25 patients with a brief educational intervention. The 12 month self-reported cessation rate in the intervention group was 56.3% vs. 11.1% in the control group ( $p<0.05$ ) [9]. While this suggested perioperative interventions could be successful, the first randomized controlled trial (RCT) to evaluate the long-term effects of smoking cessation demonstrated no difference in quit rates between patients who received counseling and nicotine replacement therapy (NRT) vs. no intervention 12 months after a variety of surgical procedures (approximately 20% in both groups) [10].

NRT can be provided in sustained form *via* transdermal patches of varying doses or short acting forms including gum, sublingual tablets, lozenges, inhalation and oral/nasal sprays. A Cochrane review concluded that “high-quality evidence” exists for all licensed forms of NRT to aide in smoking cessation efforts [11]. Regardless of setting, NRT increases the rate of stopping smoking by 50%-60% over patients who do not receive any NRT while trying to quit.

Three additional preoperative cessation program RCTs with at least 12 months of follow-up were published between 2008 and 2010 involving counseling and NRT compared to no intervention or inconsistent advice regarding the risks of smoking related to surgery [12-14]. Villebro et al. evaluated the 12 month cessation rates of smokers undergoing elective hip and knee replacements who were randomized to receive counseling and NRT or no intervention. At 12 months, the intervention group had a significantly higher rate of smoking abstinence (21.7% vs. 3.3%,  $p<0.01$ ). In this study, low nicotine dependence and having a non-smoking partner had the highest predictive value of being smoke-free at 1 year. Similarly, Sadr Azodi et al. randomized elective orthopedic and general surgery patients to weekly telephone or in person meetings and NRT vs. brief or no cessation information related to surgery. This trial demonstrated a significantly higher rate of patients in the intervention group self-reporting that they were not smoking at 1 year (32.7% vs. 14.5%,  $p<0.05$ ). In this study, low nicotine dependence and BMI >30 were significantly associated with smoking cessation 1 year after surgery. Interestingly, Thomsen et al. found no difference

in the 12-month quit rate of breast cancer surgery patients randomized to a brief course of motivational interviewing (1 interview of 45 to 90 minutes) and NRT compared to standard of care (13% vs. 9%). A systematic review and meta-analysis that primarily included the above 4 RCTs noted that the literature is supportive that preoperative interventions likely lead to more successful cessation rates  $\geq 12$  months after surgery [9].

More recently, a RCT evaluated the combination of counseling and NRT, similar to previous studies. This Canadian study, published in 2015, randomized 168 smokers undergoing a variety of elective surgeries identified in the preoperative clinic as smokers to receive brief counseling, smoking cessation brochures, referral to a Quitline and free NRT for 6 weeks to standard care, which included inconsistent perioperative cessation advice [15]. Seventy-six percent of patients were available for 12 month telephone follow-up and the self-reported rate of 7-day point prevalence (PP) of abstinence from smoking was 25.4% in the intervention group versus 8.3% in the control group ( $p<0.05$ ). Being in the intervention group and a lower nicotine dependence (Fagerstrom [16] score <4) at the time of surgery were significant predictors of successful cessation at 12 months.

## VARENICLINE

Separate from NRT, varenicline has also been investigated as a preoperative long-term cessation aide. Varenicline acts on the  $\alpha 4\beta 2$  nicotinic acetylcholine receptor as both a partial agonist and antagonist [17]. These actions reduce the rewarding effect of nicotine and also help reduce withdrawal symptoms [18]. The first preoperative RCT to study the benefits of varenicline in improving smoking cessation rates was a multi-center, double-blind placebo-controlled trial of elective ambulatory or inpatients scheduled for a variety of surgeries [19]. In this study, all patients received two 15-minute standardized counseling sessions and the target quit date was 24 hours prior to surgery. Patients were followed for 1 year *via* telephone calls and the primary outcome was 7-day PP abstinence from smoking at 12 months. They found a significant increase in the likelihood of 7-day PP of being smoke free in the varenicline group (36.4% vs. 25.2%,  $p<0.05$ ). Unlike many of the previous studies, abstinence was correlated with mailed urinary cotinine tests. This group also reported the results of a RCT comparing varenicline, counseling and a fax referral to a telephone Quitline to brief advice and self-referral to a Quitline in patients undergoing elective, non-cardiac surgery [20]. The primary outcome measure was the 7-day PP abstinence from smoking at 12 months and the secondary outcome was continuous abstinence (defined as being smoke free for the preceding 4 weeks) at 3, 6, and 12 months. The 7-day PP rate at 12 months was significantly higher with the more intensive interventions (42.4% vs. 26.2%,  $p<0.01$ ). The 4-week continuous abstinence rate was higher in this group as well at all time points measured: 3 months (34% vs. 19%,  $p<0.01$ ), 6 months (34% vs. 19%,  $p<0.01$ ) and 12 months (32% vs. 17%,  $p<0.01$ ). Participating in the more intensive smoking cessation program was significantly associated with smoking abstinence 12 months

after surgery (Relative Risk 1.58, 95% Confidence Interval 1.12-2.21;  $p < 0.01$ ).

## OTHER ADJUNCT THERAPIES

Pamphlets, brochures, e-learning modules, and web-based education programs have been utilized for smoking cessation but have not been specifically studied alone with long-term outcomes. Quitlines, where patients may call for information and support, have been included as part of programs with long-term outcomes and may be a practical way to provide additional follow-up, especially in more rural populations [21]. Text messaging related to smoking cessation has been shown to be effective overall in a meta-analysis of 20 published studies encompassing 15,593 patients [22]. However, many of these studies included other components, were not preoperative, and did not have 12-month outcomes.

Bupropion is a nicotinic acetylcholine receptor antagonist and also inhibits dopamine and norepinephrine uptake in the synaptic cleft [23]. These actions likely mitigate the stimulatory effects of nicotine on the postsynaptic membrane and reduce withdrawal symptoms and cravings, similar to varenicline. Based on RCT data with at least 12 weeks of therapy, an approximate overall smoking abstinence rate of 17% at 52 weeks with bupropion was noted [24]. Interestingly, of the 26% of patients who had quit by the end of bupropion therapy, 62.5% were still abstinent at 52 weeks. However, these studies were not limited to preoperative patients. One RCT of preoperative patients randomized to bupropion ( $n=24$ ) or placebo ( $n=23$ ) did not demonstrate a significant difference at 6 weeks after starting treatment, at the time of surgery, or at 6 months postoperatively between the two groups [25]. Based on available data, The Society for Perioperative Assessment and Quality Improvement (SPAQI) notes that there is insufficient evidence that bupropion should be provided to perioperative patients to assist with smoking cessation [21].

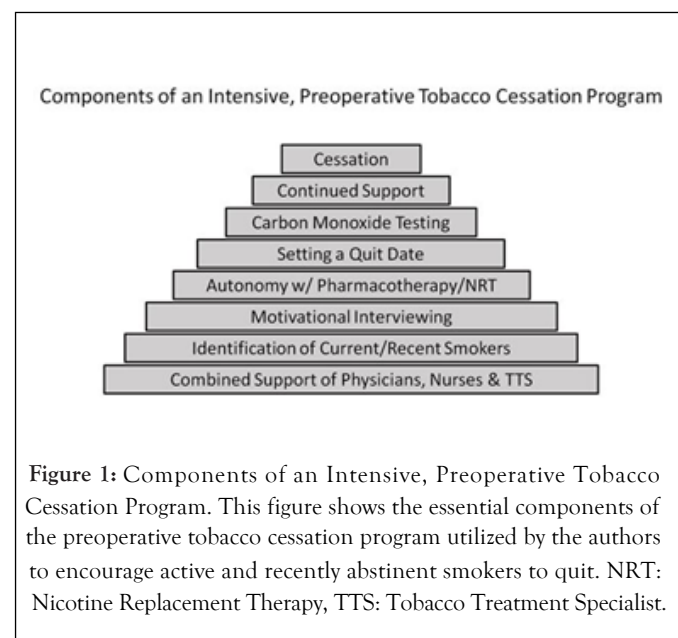
Electronic cigarettes (ECs) were intended to be a smoking cessation aide. While these devices may carry less carcinogenic material into the lungs than traditional smoking, data demonstrating their efficacy for smoking cessation are highly variable. A recent systematic review and meta-analysis concluded that due to limitations of the available studies, "it is impossible to make strong inferences regarding whether e-cigarette use promotes, has no effect or hinders smoking cessation" [26]. Based on available data, many experts would not recommend the use of ECs for cessation in the perioperative period and recommend the use of more proven pharmacotherapy [21,27].

## IMPLEMENTATION

Issues with perioperative smoking cessation are not related to a lack of efficacious interventions, but rather a lack of implementation and adoption of these interventions into routine clinical practice [2]. A lack of time, appropriate training and cessation resources have all been identified as barriers to effective preoperative tobacco cessation programs [28]. Physicians, in particular, can be

reluctant to engage patients in busy clinics or around the time of sensitive diagnoses, such as cancer. These concerns highlight the importance of collaborative, multi-disciplinary teams to facilitate smoking cessation [29].

We have recently reported the implementation and long-term outcomes (6, 12, and 24 months postoperatively) of an intensive, multi-dimensional preoperative smoking cessation program for patients undergoing lung resection (Figure 1) [30,31]. Through this program all smokers are identified and strongly encouraged by the surgeons to quit and informed their surgery may be cancelled or delayed if they continue to smoke. Smokers were also highly encouraged to meet with a certified tobacco treatment specialist (TTS) for at least a 1-hour counseling session involving motivational interviewing (an opt-out approach), and personalized pharmacotherapy. Carbon monoxide breath testing was administered at preoperative visits and on the day of surgery to verify smoking status. Patients were also given a moderate exercise regimen to follow and could have additional in-person or telephone sessions with the TTS as needed. Interventions were provided free of charge to all patients. Seventy-three percent of patients who met with a TTS used some form of NRT. Rates of cessation were 55.6% at 12 months and 51.7% at 2 years. Eighty-three percent of patients with 2 years of follow-up reported at least one successful cessation attempt. Impressively, 62% of patients who quit prior to surgery never returned to smoking, compared to just 18% who were able to quit following their operation, which was statistically significant ( $p < 0.001$ ).



A recently published small study ( $n=27$ ) demonstrated a self-reported continued smoke-free rate of 47.6% for those patients able to quit prior to total joint arthroplasty, with an average time from operation to survey of 3.7 years [32]. Similarly, of 47 patients who underwent elective cosmetic surgery with an average follow up of 63 months, 23.8% self-reported they had not smoked since surgery [33]. A recent Australian study of 50 consecutive smokers attending an outpatient pre-admission clinic prior to elective

surgery who received brief (15 minute) counseling sessions, brochures, referral to a Quitline and 2 weeks of NRT noted the 7-day PP of self-reported smoking abstinence at 12 months was 28.0% [34].

## SUMMARY

Strong data exists that the preoperative and perioperative period are opportune times to assist patients with smoking cessation. No one method has proven to be optimal in helping patients quit. Thus, it is likely that multi-factorial, personalized and multi-dimensional programs will have the highest rates of success. Regardless, one of the most important aspects of any program is conveying the importance of cessation to the patient and offering your assistance. Focusing on identifying current and recently quit smokers who are at risk of relapse and integrating cessation efforts into everyday clinical practices is also fundamental to successful implementation. In addition to the short-term benefits of decreased perioperative complications, many of these programs have a demonstrated rate of long-term successful smoking abstinence extending to at least 12 months postoperatively.

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