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Association of deferring a quit attempt with smoking cessation success: A secondary analysis☆,☆☆,★

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ABSTRACT

Several smoking cessation treatments ask smokers to wait to quit to obtain treatment. We report a secondary analysis of whether a later quit attempt is associated with less success. In a placebo-controlled trial of varenicline that allowed smokers to set their quit date within 5 weeks after starting medication, 24% had their first quit attempt during week 1, and 27%, 19%, 18% and 12% in subsequent weeks. Continuous abstinence between 9 and 24 weeks declined over time; that is, from 36% to 37%, 35%, 29%, and 18% across the 5 weeks ($p < 0.001$). The only statistically significant difference was between the last week and prior weeks. Whether a later quit attempt actually causes less success or is a marker for other variables (e.g., low motivation) is unclear.

1. Introduction

Usually those seeking treatment for non-nicotine drug disorders have ongoing psychosocial or health problems such that treatment must begin as soon as possible (Kleber et al., 2006). In contrast, most of those seeking treatment for nicotine dependence have no urgent problems. In fact, many smoking cessation interventions instruct smokers who plan to stop smoking to wait to quit for several weeks in order to receive treatment before the quit day (e.g., self-monitoring, gradual reduction, nicotine replacement therapy pretreatment, or vaccines). Most retrospective studies have reported that, in self-quitters (Cooper et al., 2010; Larabie, 2005; Sendzik, McDonald, Brown, Hammond, & Ferrence, 2011; West & Sohal, 2006) and in treatment seekers (Ferguson, Shiffman, Gitchell, Sembower, & West, 2009; Hughes & Callas, 2011), a planned quit date is associated with less success than a spontaneous quit attempt. The only experimental study of immediate versus later quitting was a small ($n = 16$/condition) randomized, controlled trial (RCT) of smokers trying to quit in the near future, done decades ago (Flaxman, 1978). It found that those randomized to the later quit condition were more, not less, successful. Finally, other studies have examined a similar, but different outcome; that is, not quitting until after the set quit date and found that this predicted worse outcomes (Kenford, Fiore, Jorenby, Smith, Wetter, & Baker, 1994; Westman, Behm, Simel, & Rose, 1997).

Given these mixed results, we conducted a secondary analysis of the effect of a later quit attempt in a recent RCT of varenicline (Rennard et al., 2012). The major asset of this study was that, in contrast to most tobacco cessation studies in which the experimenter set the quit date, this study explicitly instructed participants to self-select a quit date between 2 and 5 weeks after medication onset. We tested whether later quit attempts were associated with worse outcome.

We have used the term "later" quit attempts rather than "delayed", "deferred", or "postponed" quit attempts because these terms may connotate procrastination or noncompliance. Since our participants were explicitly told that they could set a quit date at any time point in the next 5 weeks, later quit dates in our study may not necessarily warrant this connotation.

2. Methods

This double-blind, placebo-controlled, multinational study randomized smokers interested in quitting in a 3:1 ratio to varenicline or

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placebo for 12 weeks. The methods and results of this trial are described elsewhere (Rennard et al., 2012). The study was approved by local ethics committees and was registered at www.clinicaltrials.gov (#NCT00691483).

During week 1, participants were instructed to continue smoking while varenicline was titrated to up to 1.0 mg twice daily, and this dose was then administered for up to 12 weeks from study onset. To better mimic real-world conditions, at study onset, participants were not required to set a quit day but instead were asked to choose to quit at any time between the start of the second week and the end of the fifth week after starting treatment. Participants received brief (<10 minutes) counseling at weekly visits for 12 weeks. The primary endpoint was continuous abstinence between weeks 9–24 after medication onset, and a secondary endpoint was continuous abstinence between weeks 9–12, both confirmed by carbon monoxide (CO) ≤10 ppm at each visit. A quit attempt was defined by weekly retrospective self-report and did not require 24 hours of abstinence (Hughes & Callas, 2010).

As described in the main report, varenicline increased abstinence between weeks 9–12 compared with placebo (53% vs. 19%, odds ratio [OR] = 5.9) and abstinence between weeks 9–24 (35% vs. 13%, OR = 4.4) (Rennard et al., 2012). A comparison of these results with studies not allowing flexible quit dates suggests that allowing a flexible quit approach did not decrease or increase the incidence of abstinence, nor the efficacy of varenicline versus placebo (Hughes, Russ, Arteaga, & Rennard, 2011).

Our secondary analysis examined quit attempts during weeks 1–5 because, a) even though week 1 was out of the recommended range, we thought inclusion of those who quit immediately was important, and b) we did not collect exact quit dates after week 5. We used abstinence between weeks 9–12 and weeks 9–24 as outcomes because they were the *a priori* endpoints in the main study. In addition, these outcomes would impose at least a 4-week period between a quit attempt and the beginning of the abstinence measurement period.

The 562 participants who made a quit attempt prior to the end of week 5 (82% of the 659 participants enrolled) were pooled from both treatment arms for analysis. These participants averaged 43 (standard deviation [SD] = 12) years of age, smoked 19 (8.3) cigarettes/day, and had a mean Fagerström Test for Nicotine Dependence (FTND) (Heatherton, Kozlowski, Frecker, & Fagerström, 1991) score of 5.5 (2.2). Almost half (40%) were women, and 65% were non-Hispanic Whites.

In our main analysis, a logistic regression was used to assess the effect of time to quit attempt on abstinence in weeks 9–24. We also used survival analyses to examine the effect of postponing the quit attempt on duration of abstinence of that quit attempt using the log-rank test. We used propensity scores to adjust for imbalances in measured baseline characteristics in the main analyses. Propensity scores controlled for: region, treatment assignment, average number of cigarettes per day, number of previous quit attempts (none vs. at least one), time to first cigarette in the morning, longest period of abstinence, and years of smoking. The iterative algorithm of Rosenbaum and Rubin (Rosenbaum & Rubin, 1984) was used to construct the propensity score model. Analyses were based on intent-to-treat and missing data were assumed to represent smoking.

3. Results

The mean time to the first quit attempt across all participants was 15.7 (9.7) days. Despite the protocol recommendation to wait 1 week to make a quit attempt, 24% of participants made their first quit attempt during the titration period (week 1); 27% did so during week 2; 19% during week 3; 18% during week 4; and 12% during week 5. In a univariate regression onto time-to-quit attempt, being a woman (women = 16.6 days, men = 15.0 days; $p = 0.053$), enrolled in a North American study site (North America = 17.8 days, others = 14.5 days; $p < 0.001$), having a shorter time-to-first-cigarette in the morning (≤30 min = 16.4 days, >30 min = 13.0 days; $p = 0.001$), having a higher FTND baseline score (FTND ≤ 5 = 15 days, FTND > 5 = 16.5 days; $p = 0.024$), never having been abstinent for a day in past (never abstinent = 16.5 days, prior abstinence = 13.7 days; $p = 0.002$), and placebo treatment assignment (placebo = 17.6 days, varenicline = 15.1 days) were associated with a longer time-to-first quit attempt. After adjusting for the characteristics described in the propensity analyses, none of these characteristics remained significantly correlated with time to first quit attempt and, thus, were not included as covariates in the analyses Fig 1.

In the propensity analysis regression, longer time-to-first quit attempt was associated with decreased probability of abstinence during weeks 9–12 (chi-square = 9.1, $p = 0.003$) and weeks 9–24 (chi-square = 15.5, $p < 0.001$). Treatment assignment did not interact with the effect of later attempts on success; that is, the difference in quit rates between varenicline and placebo was not influenced by early versus late quit attempts. Survival analyses examining the duration of abstinence found similar outcomes.

The propensity-score-adjusted abstinence rate for weeks 9–12 was 51% for those whom first quit during week 1 and was 52% for those who first quit during week 2, 55% for those who quit during week 3, 51% for those who quit during week 4, and 38% for those who quit during week 5. Similar results for weeks 9–24 abstinence were 36%, 37%, 35%, 29%, and 18%. In follow-up analyses, the only statistically significant difference in week 9–24 abstinence among the groups was between the last week and prior weeks and this was true for both treatment groups (all $p < 0.001$). The mean duration of first quit attempt among all participants was 27 (SD = 60) days for those who first quit during week 1, and was 52 (SD = 72) days in those who quit during week 2, and was 53 (SD = 70) days, 52 (SD = 67) days, and 34 (SD = 58) days for those who first quit during the 3 subsequent weeks.

4. Discussion

This secondary analysis of an RCT found that, when smokers themselves choose when to quit, those who did not attempt to quit until the last recommended week were less likely to achieve continuous abstinence. This result occurred in both varenicline and placebo groups and was consistent across different quit outcomes and different statistical analyses. Those who quit later differed from those who quit earlier on several outcomes; however, these did not influence the outcome of our analyses.

The only prior trial of early versus late quit attempts was a true RCT (Flaxman, 1978). This study randomized 64 smokers unto a 2 × 4 factoral design (aversive conditioning vs. attention control, crossed with gradual reduction vs. partial gradual reduction vs. abrupt with immediate quitting vs. abrupt with later target date). To examine the comparison most relevant to the current study, we ignored the aversive conditioning versus attention control contrast because results did not differ between these two groups. We also ignored the gradual cessation conditions because gradual by definition requires later quitting. In the remaining comparison of immediate versus later abrupt cessation, the abstinence rates were 13% in the former versus 56% in the later condition; that is, results opposite to ours. The major advantage of this trial was randomization to quit now versus later; however, this trial was done over 30 years ago and did not include several methodological assets such as biochemically confirmed abstinence. Also, its very small sample size ($n = 16$/group) may have produced false positive results. Unfortunately, we know of no RCT of immediate versus later quitting since that trial. Our results are consistent with most prior retrospective studies (Cooper et al., 2010; Ferguson et al., 2009; Hughes & Callas, 2010; Kenford et al.,