

Lindson-Hawley N, Banting M, West R, and et al. Gradual Versus Abrupt Smoking Cessation. A Randomized, Controlled Noninferiority Trial. *Ann Intern Med.* 2016; 164:585-592.

PMID:26975007

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Date: 6-3-16

Design: Randomized controlled noninferiority trial

Objective: To examine the success of quitting smoking by quitting gradually compared with abrupt smoking cessation.

Population /sample size/setting:

- A total of 697 adult smokers with tobacco addiction including 347 females and 350 males, (mean age 49 years) were recruited across 31 primary care practices by 23 nurses between June 2009 and December 2011 in England.
- Participants were randomized to one of two smoking cessation groups: (1) abrupt cessation group (n = 355), or (2) gradual cessation group (n =342).
- Inclusion criteria included addiction to tobacco, smoking at least 15 cigarettes or 12.5 grams of loose-leaf tobacco daily, an end-expiratory carbon monoxide (CO) concentration of at least 15 ppm, and a willingness to quit smoking 2 weeks after trial enrollment.
- Exclusion criteria included current participation in cessation treatment, contraindications to nicotine replacement therapy (NRT), participation in other medical trials, severe dependency on alcohol or illicit drugs and severe acute or chronic medical or psychiatric conditions making it unlikely that participants would be able to meet the demands of the trial, and any other circumstances precluding the ability to meet the demands of the trial.

Methods/Interventions/Outcome Measures:

- Study design was a randomized, intention-to-treat noninferiority clinical trial with 6 months of follow-up.
- Randomization to treatment was computer-based, in a 1:1 ratio to gradual or abrupt cessation group at the baseline visit using sealed, numbered envelopes in turn, and stratified by research nurse. Treatment assignment was unblinded to the participant and the research nurse. For husband and wife pairs, one person was allocated randomly and the other was allocated to the same group.
- In the gradual cessation group, participants aimed to gradually reduce tobacco use over 2 weeks before a planned quit date to half of the baseline amount by the end of the first week, and to 25% of the baseline amount by the end of the second week. They were provided with nicotine patches, 21 mg/d, and a choice of short-acting NRT products (gum, lozenges, nasal spray, sublingual tablets, inhalator, or mouth spray) during the 2 week reduction period.

- Participants in the abrupt-cessation group were asked to smoke as normal and not reduce between the baseline appointment and quit date. They stopped smoking abruptly on a planned quit day. They could use nicotine patches, 21 mg/d, but no short-acting NRT in the 2 week period before the quit date.
- Pharmacotherapy was identical in both groups from the quit day onward and consisted of a nicotine patch, 21 mg/d, plus short-acting NRT of the participant's choice.
- Both groups were provided behavioral counseling which consisted of withdrawal-oriented therapy focused on the commitment to abstain completely, and provided support early, which is when withdrawal symptoms are worst and relapse is most likely. Participants met with the research nurse a total of 8 times between 2 weeks before and 8 weeks after the quit date.
- The primary outcome was validated abstinence from smoking 4 weeks after the quit day using the Russell Standard 4 week abstinence measure. The Russell Standard allows a 2-week grace period from quit day for slips and uses an intention-to-treat approach that assumes that persons lost to follow-up are smokers. Russell Standard abstinence is confirmed by an exhaled CO concentration of less than 10 ppm. Secondary outcomes were 6-month abstinence and whether outcomes differed according to participants' preferred method of quitting.
- Baseline visits included assessments for demographic characteristics, smoking history, nicotine dependence, and preference for gradual or abrupt cessation. Follow-up assessments also included dispensing of study medications, and assessment of smoking status and use of other nicotine products, nicotine withdrawal, carbon monoxide levels, adverse events/safety, and medication adherence.
- The predetermined noninferiority margin was equal to a relative risk (RR) of 0.81 or a 19% reduction in the effectiveness of quitting gradually compared with abruptly. This is an absolute difference in quit rates of 9.5% at 4 weeks, assuming a 50% quit rate in the abrupt cessation group. Using a 1-sided alpha of 5%, 343 participants per group were needed to have 80% power to detect this 9.5% difference in the primary outcome.

Results:

- Baseline demographic characteristics and smoking-related variables appeared to be similar among the 2 groups, but specific significance levels or P values for any differences were not reported.
- Ninety-four percent of participants were white, the average number of cigarettes smoked per day was 20, and participants were equally split between men and women.
- The primary outcome, 4-week Russell Standard abstinence, was achieved by 39.2% (CI, 34.0% to 44.4%) of the gradual-cessation group and 49.0% (CI, 43.8% to 54.2%) of the abrupt-cessation group. Noninferiority was not shown (unadjusted RR, 0.80 [90% CI, 0.68 to 0.96]). But at 4 weeks, achieving abstinence was significantly less likely in the gradual-cessation group than in the abrupt-cessation group (adjusted RR, 0.80 [95% CI, 0.66 to 0.93]).
- The risk estimates for the secondary outcomes of 6-month prolonged abstinence and point prevalence abstinence, also indicated superiority of abrupt over gradual cessation. At 6 months, 15.5% (CI, 12.0% to 19.7%) of the participants in the gradual-cessation group were abstinent compared with 22.0% (CI, 18.0% to 26.6%) in the abrupt-cessation group (relative risk, 0.71 [CI, 0.46 to 0.91]).

- Participants who preferred gradual cessation were significantly less likely to be abstinent at 4 weeks than those who preferred abrupt cessation (38.3% vs 52.2%; $P = 0.007$).
- Attendance at the first clinic visit was similar between groups, but attendance at the second clinic visit was significantly better in the abrupt cessation group.
- Participants in the gradual-cessation group had reduced their cigarette consumption by an average of 48% (target of 50%) after week one of reduction, and by 68% (target of 75%) after 2 weeks of reduction.
- Medication adherence rates were generally good with over 80% of participants in both groups using their nicotine patch daily in the first 2 weeks.
- All trial medications were well tolerated, and no serious adverse events were due to the trial medication.

Authors' conclusions:

- This study showed clear evidence that quitting abruptly was superior in the short (4 weeks) and longer term (6 months). Quitting smoking abruptly is more likely to lead to lasting abstinence than cutting down first, even for smokers who initially prefer to quit by gradual reduction. The study results indicate that gradual cessation was less successful than abrupt cessation probably because fewer participants made a quit attempt when reducing smoking first.
- This study supports the conclusion that gradual cessation may be a useful way to increase cessation in the population, but abrupt quitting is the more effective method, even in persons who prefer not to quit abruptly.
- Adherence to behavioral instructions and pre-quit NRT was good, and medication was well-tolerated.
- Participants who preferred to quit gradually at baseline were less likely to achieve abstinence than those who favored abrupt quitting, regardless of how they were allocated to quit.
- Nonwhite groups formed only 6% of the trial population and thus the study results may not apply to groups other than white British persons, although there is no known mechanism that might explain effect modification by ethnic group.
- These results imply that in clinical practice, clinicians should encourage persons to stop smoking abruptly and not gradually. However, gradual cessation programs could still be worthwhile if they increase the number of persons who try to quit or take up support and medication while trying.
- Population-focused trials are needed to assess the population effect of promoting and supporting a wider range of quitting options and programs than most countries currently support. Future trials need to find ways to retain smokers in gradual cessation programs while they reduce smoking, and to discover more successful reduction methods.

Comments:

- This study supports the conclusion that abruptly quitting smoking is more effective than gradual cessation in obtaining smoking abstinence at 4 weeks and 6 months.
- One explanation for the advantage of abrupt cessation over gradual cessation could be that gradual cessation seems to deter participants from making quit attempts. Another

explanation could be that the motivation to quit predicts the means by which persons quit, and those who are less motivated seem to select gradual cessation. This study supports this explanation, since participants who favored gradual cessation at baseline were less likely to quit than those who favored abrupt quitting, regardless of allocation.

- Strengths of this study included behavioral counseling that guided participants on how to reduce smoking using structured plans, which seems to enhance the success of reduction and subsequent cessation. Additional strengths include trial registration, allocation concealment, long term follow-up, adequate sample size, an appropriate randomization description, and a clearly designated primary outcome.
- The authors conducted a sensitivity analysis excluding the member of the couple who was non-randomly assigned to account for non-independent observations, and the results were similar for abstinence at 4 weeks and 6 months.
- Limitations of this study include a homogenous, almost all white population, and the failure to include a baseline smoking variable on total years of smoking.
- The authors failed to acknowledge that the results of this study probably only apply to smokers who are motivated to quit smoking.
- Even though the quit rates in this study are not that good, they appear to be similar to previous studies.
- The authors failed to include P values to show if there were any significant differences between the 3 groups in the baseline demographic and smoking related variables.
- The results of this study call into question whether clinicians should even support gradual smoking cessation programs, and should rather persuade their patients to abruptly quit.

Assessment:

This adequate study provides some evidence that among adults motivated to quit smoking, abrupt smoking cessation is the more effective method that leads to lasting abstinence over a period of 4 weeks to 6 months compared to gradual cessation, even for smokers who initially prefer to quit by gradual reduction.