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REVIEW ARTICLE

Smoking Cessation for Smokers Not Ready to Quit: Meta-analysis and Cost-effectiveness Analysis

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Context: To provide a systematic review and cost-effectiveness analysis on smoking interventions targeting smokers not ready to quit, a population that makes up approximately 32% of current smokers.

Evidence acquisition: Twenty-two studies on pharmacological, behavioral, and combination smoking-cessation interventions targeting smokers not ready to quit (defined as those who reported they were not ready to quit at the time of the study) published between 2000 and 2017 were analyzed. The effectiveness (measured by the number needed to treat) and cost effectiveness (measured by costs per quit) of interventions were calculated. All data collection and analyses were performed in 2017.

Evidence synthesis: Smoking interventions targeting smokers not ready to quit can be as effective as similar interventions for smokers ready to quit; however, costs of intervening on this group may be higher for some intervention types. The most cost-effective interventions identified for this group were those using varenicline and those using behavioral interventions.

Conclusions: Updating clinical recommendations to provide cessation interventions for this group is recommended. Further research on development of cost-effective treatments and effective strategies for recruitment and outreach for this group are needed. Additional studies may allow for more nuanced comparisons of treatment types among this group.

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CONTEXT

Despite declining smoking rates, smoking remains the single largest cause of preventable disease and death.[1] Although the majority of smokers would like to quit sometime in the future, only 68% to 69% of smokers report willingness to quit within a year.[1,2] Most smoking-cessation literature focuses on those ready to set a quit date.[2,3] In fact, the clinical practice guidelines devote nearly 250 pages and provide scores of supporting tables for smokers ready to quit smoking, whereas spending only three and a half pages and one supporting table on smokers not ready to quit (SNRTQ).[4] The current clinical practice guidelines for SNRTQ recommend motivational interviewing (MI) to encourage these smokers to consider quitting, but do not make further recommendations for this group until they express a motivation to quit.[1,5]

Research examining differences between SNRTQ and those ready to make a quit attempt find that many of the behavioral differences between these groups, such as self-efficacy to cope with temptation to smoke, support of quit attempts by significant other, and use of nicotine replacement therapy (NRT), can be addressed directly through interventions.[6] Currently, the most validated and widely studied method for treating SNRTQ is combined behavioral and pharmacological rate reduction, used as an approach to produce initial reductions in tobacco use and to enhance self-efficacy for ultimate smoking cessation.[7–9] Combined behavioral/pharmacological rate reduction has

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been shown in a meta-analysis to more than double the odds of cessation in SNRTQ.[10] However, since the writing of this meta-analysis, the treatment field has taken considerable leaps forward, both in terms of pharmacological interventions and combined pharmacological and behavioral treatments for SNRTQ.[11,12] Additionally, because the types and intensity of studies targeting SNRTQ may differ from smokers ready to quit, it is important to evaluate the cost effectiveness in conjunction with the efficacy of interventions in this difficult to treat group of smokers.

This study combines a systematic review to estimate the effectiveness of pharmacological, behavioral, and combination smoking-cessation interventions targeted towards SNRTQ with a cost-effectiveness analysis to examine the most economical methods for intervening on this group. Effectiveness is expressed in the estimated number needed to treat (NNT) in order to produce one additional quit, and cost effectiveness is expressed by the estimated cost per quit. Although many factors that promote smoking in those ready to quit and those not ready to quit are likely to be similar, it is hypothesized that the intensity, and thereby the cost of interventions (cost per quit) would be higher than typically found in the literature on smokers ready to quit.[10]

EVIDENCE ACQUISITION

Search Strategy

Studies of interventions targeting SNRTQ were reviewed. SNRTQ were defined as smokers who are either in the pre-contemplation (not thinking about quitting within the next 6 months) or contemplation (thinking about quitting but not ready to quit within the next 6 months) stage of the Transtheoretical or Stages of Change Model; these groups combined make up between 32% and 46% of current smokers.[2] Ten papers reviewed in a previous study by Asfar et al.[10] are summarized in Appendix Table 1 (available online).[13–22] A search for additional clinical trials published after the Asfar et al.[10] review was performed (between 2011 and 2017), using MEDLINE and Google Scholar and the search terms *smoking*, *smoker*, or *smokers* with the phrases *not ready* or *unmotivated* and *quit*.[5]

Selection Criteria

This search yielded 619 initial results; 12 of which met the criteria as RCTs that specifically recruited adult (aged ≥18 years) smokers who were not ready or willing to quit immediately, within the next 30 days, or within the next 6 months. Ten of these studies are summarized in Appendix Table 2 (available online). Two were excluded and are discussed below.

Including studies from Asfar et al.[10] and the new literature search, 20 studies in total were reviewed, 15 of which had abstinence outcomes that were biochemically verified and were therefore included in the meta-analysis (Figure 1). Studies examined pharmacological interventions, behavioral interventions, or combinations of these two, and were grouped according to intervention type. Interventions using other types of tobacco, such as smokeless tobacco, snus, or e-cigarettes were not included. Each study had one comparison group, which received placebo, usual care, or no treatment, noted in Appendix Tables 1 and 2 (available online). Studies with multiple treatment arms compared pooled treatments against the control group.

Primary Outcome Definition

Included studies measured smoking abstinence, or quits, using either continuous abstinence or point prevalence (PP) measures, which were either self-reported or biochemically verified by cotinine levels in saliva, urine, or carbon monoxide exhalation. If available, 7-day PP outcomes were reported.

One author performed the searches and abstracted data from included studies into a spreadsheet; a second author checked abstracted data for accuracy. The study design was registered as a systematic review in PROSPERO. All data collection and analyses were performed in 2017.

Calculation of Efficacy Estimates

For each study, an OR, representing the odds of quitting for participants in the treatment group relative to the control group, with a 95% CI, was calculated using the reported number of quits and the reported sample size in both treatment and control groups. In this case, an OR >1 indicated that participants in the intervention group were more likely than participants in the control group to achieve quitting. Summary, or pooled effects across studies in each treatment type were calculated as the weighted mean of individual ORs.[23] To minimize risk of bias, the summary measures were calculated using only studies with biochemically validated outcomes; funnel plots and statistical tests for small-study bias were estimated.

The measure I^2 was used to assess whether heterogeneity of effect sizes was due to more than would be expected from sampling error alone.[24] Moderator analysis to estimate the effect of study design factors on the estimated effect size was conducted and reported in the footnote of Table 2 and Appendix Table 3 (available online). Potential moderators included variations in study design features, such as: sampling individuals willing to reduce smoking, months of treatment, duration and number of treatment sessions, inclusion of secondary treatments given to both treatment and control subjects, usual care versus no treatment in the control group, and inclusion of clinic visits as part of the study protocol.

For each study, the number of observations from the full sample of smokers and number of quits in both treatment and control interventions were used to calculate the NNT.[25] Summary NNT for each of the three intervention types was calculated, using only studies with biochemically validated outcomes. Efficiency estimates assumed that smokers lost to follow-up have resumed smoking and did not quit.

Calculation of Cost Estimates

Cost effectiveness was measured by cost per smoker and cost per quit. To make these calculations, costs were compiled from various sources for each of the types of pharmacological and behavioral interventions. Table 1 shows the estimated cost for a 1-month supply of pharmacological therapies and an average cost for each type of behavioral intervention. Assumptions used to determine costs are described in Table 1. These costs are used in Table 2 to estimate cost per smoker and cost per quit of each study. Appendix Table 5 (available online) shows additional details of