Published in final edited form as:

Curr Drug Abuse Rev. 2008 June ; 1(2): 142–155.

SMOKING CESSATION FOR ADOLESCENTS: A REVIEW OF PHARMACOLOGICAL AND PSYCHOSOCIAL TREATMENTS

TS Schepis, PhD* and U Rao, MD

Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9101

Abstract

Unlike the vast literature on smoking cessation in adults, research in adolescents has gained significant attention only within the last decade. Even with this increase in focus, research into pharmacological aids for smoking cessation in adolescents (e.g., nicotine replacement therapy, bupropion) is a more recent phenomenon and has produced only modest results. While more extensive, much of the research on behaviorally- or psychosocially-based adolescent smoking cessation interventions has been limited by a lack of control for contact time, biochemical verification of self-reported abstinence, and/or a theoretical focus for the interventions. The MEDLINE, PubMed, PSYCInfo CINHALL and Cochrane Systematic Review databases were searched for articles relevant to adolescent smoking cessation treatment. After briefly examining the adolescent smoking cessation research prior to 2000, more recent developments in pharmacological aids and psychological treatment will be reviewed. Investigations have made progress in elucidating efficacious treatments for adolescent smokers, but much work remains to be done in both pharmacological and non-pharmacological areas of treatment. With the current state of the literature as a guide, future directions for research into smoking cessation for adolescents will be proposed.

Keywords

Adolescent; smoking cessation; bupropion; behavioral treatment; nicotine replacement therapy; tobacco

Introduction

In 2000, the Department of Health and Human Services (DHHS) made the reduction of adolescent smoking rates one of its goals for the Healthy People 2010 initiative, reflecting its prominence as a public health concern¹. Indeed, smoking in this age group is associated with significant immediate and long-term problems. To illustrate, over 80% of adult smokers initiate the behavior before the age of 18², and smoking initiation in early adolescence predicts higher rates of smoking in adulthood and a reduced probability of quitting^{3–5}. The

Correspondence should be addressed to: Uma Rao, MD, Department of Psychiatry, The University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, Texas 75390-9101, Phone: 214-648-5288, Fax: 214-648-5242, uma.rao@utsouthwestern.edu.

No conflicts of interest were noted by either author.

Centers for Disease Control and Prevention (CDC) estimated that adolescent smoking will result in at least 64 million years of lost life and more than 200 billion dollars in smoking-related medical costs per year⁶. Over one-third of adolescent smokers are expected to die prematurely as a consequence of smoking⁶. Tobacco use is associated with the initiation of other addictive drug use^{7–10}, and numerous studies have linked smoking and psychiatric illness in adolescents cf.,^{11, 12, 13}. Finally, adolescent smokers experience negative health effects and decreased quality of life as a result of smoking^{2, 8, 14, 15}

Perhaps because of the detrimental consequences of smoking, 65% of high school smokers endorsed a strong desire to stop and over 55% had made a quit attempt in the past year^{16, 17}. Despite the high rate of quit attempts, no investigation has found a natural cessation rate above 11% in adolescents^{18, 19}. Furthermore, only 43% of adolescent smokers are confident that they will ever cease permanently²⁰; a significant majority (74%) reported that they believed abstinence would be “really hard”²¹. In combination, it appears that many adolescents want to stop smoking but are deterred by concerns about the difficulty of cessation.

While the risk factors for adolescent smoking are becoming better established²², research on interventions for adolescent smoking cessation is still in the early stages of development^{23, 24}. This review will focus on recent progress in adolescent smoking cessation research, examining both pharmacological and behavioral treatments. Extending research from adults, pharmacological investigations have tested nicotine replacement therapy (NRT) and bupropion as cessation aids. Only seven reports on pharmacological treatment were found; a greater number of published reports exist for behavioral treatments, but both sets of research have limitations that restrict the conclusions that can be drawn. Following the review of the current literature, future directions for research will be proposed.

Materials and Methods

A keyword search of four databases was conducted in May of 2006 using the library resources at the University of Texas Southwestern Medical Center at Dallas and repeated in July of 2007 using the library resources of Yale University. This search utilized the MEDLINE, PubMed, PSYCInfo and CINHALL databases, and searches were limited to articles published in English. In all databases, the terms “smoking cessation” and “adolescent OR teen” were entered as the initial search. Due to the large size of the returned results (e.g., 991 from MEDLINE), many of which were not germane to the review, the searches were limited by the separate use of nine terms: “treatment” “bupropion”, “nicotine replacement therapy”, “behavioral”, “internet”, “telephone”, “contingency management”, “motivational interviewing”, and “psychosocial”. Furthermore, behavioral treatment searches were limited to articles published in or after 2000, as the review by Sussman²⁵ examined the period prior to 2000.

Due to the small number of articles returned concerning pharmacological treatments, all articles employing the use of pharmacological aids were included. Furthermore, the 2001–2007 abstract databases of the annual meeting of the Society for Research on Nicotine and

Tobacco were searched for adolescent smoking cessation abstracts involving pharmacological aids. One data set (producing two abstracts) was included following consultation with the primary investigator. Behavioral or psychosocial treatment articles were only included if they concerned either programs or theoretical orientations with multiple reports. Innovative treatments, such as phone or internet cessation programs, were included even if only one published report was found, due to the limited literature in this area. Articles were prioritized if they included a treatment with a theoretical rationale, a control condition for comparison and/or follow-up cessation rate data. All studies employed biochemical verification of cessation status, with the exception of two of the psychosocial treatment studies.

Results

Pharmacological Treatment

Following the lead of research on pharmacological treatments for adult smokers please see^{26, 27, 28} for a detailed review, smoking cessation research in adolescents has concentrated on two treatments: NRT and bupropion. Table 1 (below) describes the design and outcome characteristics of the seven published pharmacological intervention studies for smoking cessation in adolescents.

Nicotine Replacement Therapy in Adolescents

Smith and collaborators²⁹ conducted the first published investigation of NRT in adolescents, testing the safety and efficacy of open-label patch treatment in 22 Caucasian adolescents. While cessation rates were low (14% at the end of eight weeks of treatment and 4.5% at six-month follow-up) and the rates of adverse events were high, this investigation gave preliminary evidence of the safety and modest efficacy of NRT in treatment-seeking adolescents²⁹. In a larger open-label trial of NRT in 101 predominately Caucasian (95%) adolescents, Hurt and colleagues³⁰ reported that 10.9% of participants were abstinent at Week 6 and 4.5% were abstinent at the six-month follow-up assessment. During the course of the study, 30 adolescents (29.7%) dropped-out of treatment, with five leaving treatment due to patch-related adverse events³⁰.

The first randomized, double-blind, placebo-controlled study of NRT³¹ treated 100 adolescents (86.9% Caucasian) using the nicotine patch. While individuals receiving active NRT treatment had significantly lower craving and withdrawal scores, no significant differences in efficacy were found between the treatment groups. Point-prevalence abstinence rates were very high (70%) after one week of treatment, and at the end of the study (11 weeks), 28% of those receiving active treatment and 24% of those receiving placebo had biochemically verified abstinence. The study employed brief individual weekly cognitive-behavioral therapy (CBT) sessions in addition to an escalating-reward contingency management (CM) paradigm³¹, which may have masked differences between placebo and NRT. Given the efficacy of CM^{32, 33} and of CBT³⁴ in fostering abstinence, it is difficult to attribute a specific portion of the treatment effect to NRT.

Finally, Moolchan et al.³⁵ used 12 weeks of either nicotine gum or patch in 120 adolescents (72% Caucasian) using a randomized, double-blind, placebo-controlled design. Study participants also received a group CBT cessation treatment, described by Moolchan and Ruckel³⁶. Participants on the patch had the highest biochemically verified abstinence rate at the end of treatment (20.6%), but this was only significantly different at a trend level from the gum (8.7%) or placebo (5%) rates. At three-month follow-up, no significant differences were seen between groups, with cessation rates maintained from the end of treatment. The continuous abstinence rate at the 3-month follow-up, defined as abstinence at all time points from Week 2 to follow-up, was highest for individuals in the patch group (17.7%); this was a significantly greater rate than that of participants receiving gum (6.5%) or placebo (2.5%). NRT-related adverse events were similar to those previously seen; at least one-quarter of the participants reported one or more symptoms, including nausea, headaches, fatigue, and dizziness³⁵.

Bupropion Administration in Adolescents

The other major pharmacological aid for smoking cessation in adults is bupropion, which is marketed under the trade names Wellbutrin (for depression) or Zyban (for smoking cessation). The initial investigation was conducted by Upadhyaya and collaborators³⁷, who investigated a seven-week open-label trial of 150 mg of bupropion to evaluate its safety and efficacy in adolescent smokers. Sixteen adolescents (87.5% Caucasian), 11 of whom had attention-deficit hyperactivity disorder (ADHD), received 300mg of bupropion and two brief cessation-related counseling sessions. At the end of treatment, there were significant decreases in both the number of cigarettes smoked by participants and their exhaled CO levels. Five of the 16 participants (31.3%) were abstinent after four weeks of medication; however, the end of treatment cessation rate was not specified. Only 9 of 16 (56.3%) participants completed at least 4 weeks of the study, with three dropping out due to adverse events. The most common adverse events reported were headache (43.8%) and insomnia (37.5%); finally, participants did not experience significant weight gain during the study³⁷.

The first placebo-controlled study of bupropion³⁸ examined a 90 day treatment using a 150mg dose in 22 older adolescents (ethnicity not given), all of whom received an unspecified behavioral intervention. Many aspects of this study make interpretation difficult, including the use of NRT prior to bupropion treatment, and the high level of depressive symptoms in participants. Also, for those who relapsed, the definition of abstinence (<15 cigarettes in the three prior days) prior to relapse is not a standard criterion in the field. That said, the study found that the adverse event rate was low and that 55% of participants (6 of 11) receiving bupropion were abstinent throughout the trial. The study also found that participants were able to maintain cessation longer on bupropion than on placebo³⁸.

More recent results presented at the 2005 Annual Meeting of the Society for Research on Nicotine and Tobacco showed that 300 mg of bupropion was superior to either a 150 mg dose or placebo after six weeks of treatment³⁹. This study examined 312 adolescents, using a randomized, double-blind, placebo-controlled design. Participants smoked a half pack per day and had two previous failed quit attempts (M. L. Muramoto, personal communication, August 2, 2006). At the end of active treatment, 16.9% of participants on 300 mg of

bupropion were abstinent, compared to 10.3% for 150 mg and 6.7% for placebo. By Week 26 follow-up, these differences had disappeared, with 10.8% abstinent on the 300mg dose, 3% on the 150mg dose and 10% abstinent on placebo³⁹. In all, this study indicated that 300 mg was well tolerated in adolescents and that 300 mg appeared to be the necessary dose to achieve a comparable cessation rate to NRT in adolescents (M. L. Muramoto, personal communication, August 2, 2006).

Following adult studies on the combination of NRT and bupropion e.g.,⁴⁰, Killen and colleagues⁴¹ examined the use of nicotine patch and 150 mg of bupropion for adolescent smoking cessation. Two hundred and eleven participants (50.2% Caucasian) were given the nicotine patch and randomized to either 150 mg bupropion or placebo for 10 weeks. No differences in verified abstinence were found between the groups at Week 10 or Week 26. At week 10 (end of treatment), 28% of the NRT plus placebo group and 23% of the NRT plus bupropion group were abstinent; at Week 26, these rates dropped to 7% and 8%, respectively. Participants with a detectable level of bupropion metabolite at Week 5 had a significantly higher abstinence rate than participants without a detectable level, and overall adherence to both NRT and bupropion was low. Together, this implies that bupropion might have aided in quitting smoking when it was taken appropriately⁴¹.

Psychosocial Treatment

Behavioral interventions have been the mainstay of adolescent smoking cessation treatment over the past two decades. Many behavioral interventions include aspects of CBT, motivational interviewing (MI), contingency management (CM), and/or the Transtheoretical model of Behavior Change. For further review of these theoretical approaches, please see^{42, 43}. Sussman²⁵ published an excellent review of behavioral treatments for adolescent cessation, focused on interventions published up to 2000. Therefore, this paper will concentrate on the literature published since that review. Sussman²⁵ found that the unweighted mean cessation rate was 14% at the end of active treatment and 12% at follow-up for active programs, compared to 7% for control conditions at both time points. The highest cessation rates were associated with MI (19%) or CM (17%); this effect was also seen in follow-up assessment. Other theoretical orientations, including social influence models, the Transtheoretical Model, affect-based approaches, and cigarette supply reduction approaches were associated with lower rates of abstinence (from 0% to 12%). Sussman²⁵ also noted that classroom-based, school clinic-based, and “computer-type” programs all showed promise.

In terms of methodology, wide variations were found in follow-up assessment (including no post-treatment measurement), many studies had missing data, and there were a large number of uncontrolled studies. Also, the variability in measured time points and in length of treatment was such that conclusions about optimal treatment duration could not be drawn. Overall, though, active interventions were associated with a near doubling of quit rates when compared to control conditions, despite the limitations noted above²⁵. A more recent Cochrane Systematic Review²⁴ examined 15 interventions, and found evidence for efficacy in approaches using the Transtheoretical Model and limited evidence supporting an intervention examined in the current paper, the Not-on-Tobacco program. The review noted

many methodological weaknesses in adolescent smoking cessation trials, namely small samples, a lack of long-term follow-up data, a lack of biochemical verification and high attrition. This manuscript will build on the results of the Cochrane review and will expand on these findings by including different studies that were not examined in that review.

Since 2000, behavioral treatments have expanded into investigations of telephone and internet-based interventions, in addition to continuing investigation of the standard treatments described above. Table 2 (below) lists the design characteristics of the psychosocial interventions for smoking cessation in adolescents examined in the current review.

Project EX

Project EX is an eight-session high school clinic-based cessation program, and it is one of two model programs recognized by the Substance Abuse and Mental Health Services Administration (SAMHSA)⁴⁴. Sussman and collaborators⁴⁵ developed the six-week, eight-session intervention based on input from focus groups of high school students; Project EX is composed of cognitive-behavioral and MI interventions, including assertiveness training, withdrawal management, psychoeducation and relapse prevention modules. The modules were presented in unique ways, such as a game show, to engage participants. Finally, before implementation, the intervention was pilot-tested for acceptability and usefulness⁴⁵.

The initial investigation of Project EX in 335 adolescents (27% Caucasian) compared three conditions: (1) a standard care control, (2) the clinic-based Project EX only or, (3) Project EX and a “school-as-community” (SAC) component⁴⁵. The SAC intervention was developed from previous investigations⁴⁶ and consisted of anti-tobacco messages disseminated in a variety of formats in school⁴⁵. Details of the standard care control were not provided. At the end of treatment, no differences were found between the two active treatment groups on cessation rate (14%), and no information was provided on the efficacy of the control condition. At the three-month follow-up, there was a significant difference between the pooled cessation rate of the active interventions (30%) and the control condition (16%). After using intent-to-treat analysis and adjusting for biochemical verification, 17% of the Project EX group achieved abstinence, compared to 8% in the control group; this difference remained significant⁴⁵. Further analyses indicated that Project EX is effective in increasing participants’ motivation to quit, which mediated cessation⁴⁷.

Project EX was examined in a sample of 46 Chinese adolescents, using an open-label design adapted to a Chinese population⁴⁸. At the end of the eight-session intervention, 3.8% had not smoked in the past 30 days and 12.4% had not smoked in the past week; at the four-month follow-up, 10.5% had been continuously abstinent for 30 days and 14.3% had been abstinent for the past week. Overall, participants reduced smoking by 16% at the end of treatment and by one-third at the four-month follow-up⁴⁸. Finally, a recent article⁴⁹ provided some evidence that Project EX could be successfully adapted to a classroom-based setting from the traditional school clinic-based setting.

Not-On-Tobacco (NOT)

The other intervention recognized by SAMHSA is the Not-on-Tobacco (NOT) program⁴⁴, which is a 10-week treatment developed by the American Lung Association. The NOT program consists of ten 50-minute sessions delivered in single-gender groups by same-gender facilitators; the sessions include cognitive-behavioral and MI topics such as the consequences of smoking, motivational enhancement, skills-training for coping with withdrawal symptoms and craving, relapse prevention, stress management, coping with peer pressure, and lifestyle modification. NOT also includes four booster sessions to prevent relapse⁵⁰. Two studies of the NOT program published in 2001 indicated that NOT may be more effective than brief, standard care^{50, 51}. One of the studies⁵⁰, examined 566 adolescents (81.3% Caucasian) and compared NOT to a 20-minute brief intervention (BI). No information was given about the cessation rates at the end of treatment, but at a follow-up assessment 7.3 months after baseline, 21.7% of NOT participants and 12.6% of BI participants had achieved cessation. NOT treatment was also significantly more effective than BI in bringing about reductions in smoking levels⁵⁰.

The second study⁵¹ examined 346 adolescents (87.3% Caucasian); in this study, 17.3% of individuals in the NOT treatment and 11.3% of individuals receiving BI achieved cessation at a three-month follow-up. These rates increased to 19.4% for NOT and 11.7% for BI at a 5.5-month follow-up assessment. At both points, the NOT program produced greater reductions in smoking than the BI, although the differences were not statistically significant⁵¹. Interestingly, it appeared that NOT was more effective for females (NOT: 29.6%; BI: 8.9%), than males (NOT: 14.4%; BI: 15.9%)⁵⁰. Further evaluation of the NOT program has continued to show its efficacy, especially in facilitating smoking reduction, although cessation rates have not always been significantly better than BI. A comparison of NOT to BI in 258 (93.4% Caucasian) adolescents found that a significantly greater proportion of NOT (8.1%) than BI participants (2.2%) had quit three-months post-baseline; the NOT rates continued to be higher at six-months (8.1% NOT; 4.5% BI) and 15-months (10.5% NOT; 8.2% BI) post-baseline, but neither was significant. Again, females (after three months, NOT: 12.2%; BI: 1.4%) appeared to benefit more than males (NOT: 4.3%; BI: 2.0%) from NOT⁵². The authors have proposed that BI may be more effective in males, resulting in BI confounding the comparison by failing to act as a true control⁵¹. Another potential explanation involves the single-gender treatment groups, which could benefit females more than males.

Horn et al.⁵³ modified NOT for use with American-Indian adolescents by including culturally appropriate materials. This modified NOT program was evaluated in 74 adolescents; at three-months post-baseline, 17.6% of males in NOT were abstinent compared to 10% of males in BI, a non-significant difference. No females ceased smoking, which was the opposite of the pattern generally seen in NOT intervention studies. Overall, a greater percentage of individuals in BI reduced smoking, whereas among those who reduced smoking, NOT was associated with greater reductions⁵³. Finally, a recent investigation indicated that combining NOT with access to an internet website containing motivational and informational materials targeted to teens boosted quit rates somewhat over the NOT

treatment alone. The main impact of the website appeared to be in boosting initial quit rates, as opposed to maintaining long-term abstinence⁵⁴.

Contingency Management

Contingency management (CM) is a behavioral intervention that reinforces abstinence using immediate and tangible rewards, often money. CM has demonstrated efficacy in adult smokers⁵⁵, and three studies have pilot-tested CM in adolescents. Corby et al.⁵⁶ conducted a three week within-subject reversal design (ABA design) experiment on eight older adolescents (ethnicity not given) to demonstrate the potential efficacy of CM. Participants were rewarded only for CO levels below 9 ppm in Week 2 of the experiment, and they were rewarded for attending sessions in Weeks 1 and 3, regardless of smoking status. Mean consecutive abstinent visits were highest during week 2 (9.5), which was significantly greater than Week 1 (0.4) but not Week 3 (5.0). Mean CO level was lowest in Week 2 (4.3 ppm); again, this was significantly different from Week 1 (16.9 ppm) but not Week 3 (9.0 ppm)⁵⁶.

Roll³² conducted a follow-up study using 22 adolescents (68.2% Caucasian), with participants assigned to either an attendance only or an abstinence group for a four-week intervention. Individuals in the attendance group were paid for daily clinic attendance regardless of smoking behavior, whereas individuals in the abstinence group were paid only if they provided breath samples with CO levels below 6 ppm. At the end of the intervention, 50% of the abstinence group had achieved four weeks of continuous abstinence, compared to 10% in attendance group. In addition, relapse following a week of continuous abstinence was greater in the attendance (50%) than the abstinence group (12%). At one-month post-treatment follow-up, 66% of individuals in the abstinence group and 40% of the attendance group were abstinent. All of these were significant differences³². The final CM study³³ compared the combination of abstinence-based CM and weekly CBT treatment to weekly CBT treatment alone in 28 adolescents. Both treatments were one month in length. After one week, the combined CM and CBT group had a higher biochemically verified cessation rate (76.7%) than the CBT group (7.2%); this was significant and persisted through the end of treatment, with 53% of CM plus CBT participants abstinent compared to 0% in the CBT-only group³³.

SMART: a workplace-based intervention

Not all programs have produced positive results, though. One interesting program was the SMART intervention, a workplace-based intervention for teen smokers^{57–60}. Given that over 70% of juniors and seniors worked at some point during the year⁶¹, the SMART program appeared able to reach many adolescents, particularly those not in school. The SMART intervention was developed from focus groups composed of working teens and included interactive interventions (e.g., games, contests) and non-interactive events (e.g., bulletin board postings, handouts). The intervention was based on social influence principles and was aimed at four domains or factors believed to contribute to smoking: social/environmental factors, personal factors, behavioral factors, and life skills.

Two studies examined the feasibility of the SMART intervention, but neither produced encouraging results^{58, 59}. Hunt and colleagues⁵⁹ found that while 84% of eligible teens were aware of the intervention, each intervention activity had a mean participation rate of 14% and only 39% of eligible individuals participated in interactive activities. Analysis of the program, using 308 adolescents (66.9% Caucasian) found a non-significant increase in intention to quit smoking (active treatment baseline: 40.6%, post-treatment: 52.8%; control baseline: 51.9%, post-treatment: 50.3%; OR = 1.75) and non-significant decreases in individuals currently smoking (active treatment baseline: 31.9%, post-treatment: 23.0%; control baseline: 22.4%, post-treatment: 20.2%; OR = 1.38), compared to control sites. There was also a reduction in the number of individuals who smoked over 20 cigarettes in the past month (active treatment baseline: 14.3%, post-treatment: 10.9%; control baseline: 10.0%, post-treatment: 10.9%; OR = 1.49) in the intervention worksites, compared to control sites⁶⁰.

Motivational Interviewing

Another intervention that has met with mixed results is motivational interviewing (MI). MI acts to resolve ambivalence and increase motivation to achieve cessation through non-confrontational exploration⁶². Since 1999, five studies have compared MI to a brief advice (BA) or standard care control condition^{63–67}; while all have found some evidence of a treatment effect, few significant results were found. Brown et al.⁶⁴ examined the efficacy of two 45-minute MI sessions in 191 adolescents (94.8% Caucasian) hospitalized for psychiatric or substance use disorders. No significant differences were found in biochemically verified point-prevalence abstinence at one-month (MI: 11%, BA: 11%), six-month (MI: 13.3%, BA: 8.5%), and 12-month (MI: 14.0%, BA: 9.9%) post-intervention assessments. MI was most effective in adolescents who were more ambivalent about attempting cessation, whereas BA was most effective with adolescents actively contemplating cessation. Colby and collaborators⁶⁵ compared MI to BA in 85 adolescents (55% Caucasian) seen in hospital settings. Participants received either a single 35-minute MI session or 5 minutes of BA; each group received a brief “booster” follow-up call. At the one-month (MI: 2%, BA: 0%), three-month (MI: 5%, BA: 0%) and six-month (MI: 9%, BA: 2%) follow-up assessments, there were no significant differences in seven-day abstinence rates. MI did appear to increase motivation to quit smoking over BA⁶⁵.

Helstrom and collaborators⁶⁶ evaluated the efficacy of a one-hour MI session in 81 adolescents (79% Caucasian) who were enrolled in treatment as part of a program for adolescents involved with the criminal justice system. Both MI and an educational control intervention were associated with roughly 6% abstinence rate based on seven-day biochemically verified abstinence at one-month post-treatment assessment; this climbed to roughly 8% for each group at the six-month post-intervention assessment. Neither difference was significant. Interestingly, participants with lower rates of alcohol use and lower levels of impulsive sensation seeking benefited more from MI, whereas those with greater alcohol use and/or impulsive sensation seeking benefited most from the educational intervention. Two other recent studies^{63, 67} have also examined MI for adolescent smoking cessation, and both found only limited efficacy for MI. As both of these studies did not verify abstinence biochemically, however, they will not be explored further here. Evidence indicates that

adolescent smokers may overreport abstinence^{45, 68}, which could confound the results of studies that do not use biochemical verification.

Phone-Based Treatment

In the last two decades, many states have instituted free telephone cessation counseling services, often called Quitlines^{69–71}. Telephone-based treatment is an inventive and potentially effective please see^{71, 72, 73} way to offer cessation services to individuals living in communities where in-person services are not available. That said, much of the available literature on telephone counseling for smoking cessation, examined only adults cf.,^{74, 75} or did not specify the age range of the participants cf.,⁷⁰. Two recent publications were found that examined the use of telephone counseling for adolescent smoking cessation.

Lipkus et al.⁷⁶ studied whether adding three telephone cessation counseling sessions to self-help materials had greater efficacy than self-help materials alone in 402 adolescents (82% Caucasian). At both time points studied, four months and eight months post-baseline, no significant differences existed between the groups. At four months, the self-help only group had 11% cessation rate, and the self-help and phone counseling group had 16% cessation rate. The rates at 8 months rose to 19% and 21%, respectively. A potential limitation of this study was that only 36% of teens completed all three calls. Biochemical verification of abstinence was attempted using salivary cotinine, but it was not included in analyses⁷⁶. Tedeschi and colleagues⁷⁷ composed an excellent article on telephone-delivered counseling for adolescent cessation. For individuals interested in a succinct cessation intervention, this article could serve as a good guide. Unfortunately, no further analysis of this intervention is available in the literature, although the authors noted that evidence for the efficacy of the intervention was presented at a National Cancer Institute symposium in 2003⁷⁷.

Internet-Based Treatment

As with telephone-based cessation interventions, internet-based treatment has garnered interest as a way to offer treatment to individuals without access to in-person treatment. Given the widespread use of the internet by adolescents⁷⁸, examining internet-based cessation treatment is a logical step towards increasing treatment availability. Woodruff and colleagues⁷⁹ performed the first study of internet treatment using only adolescent participants, investigating the efficacy of chat room-based smoking cessation therapy in 26 adolescents (55% Caucasian). Pilot testing of the seven-session MI-based intervention revealed increases in self-reported abstinence from end of treatment (22.2%) to the one-month follow-up (33.3%) up⁷⁹. A larger-scale follow-up trial⁸⁰ compared the intervention to a no-treatment control condition in 136 adolescent smokers (28% Caucasian). Participants in the active treatment (35%) were more likely to be abstinent at the end of treatment than those in the no-treatment control condition (22%), but active treatment was not superior at either a three-month (39% cessation in active treatment; 47% cessation in no-treatment control) or 12-month follow-up assessment (37% cessation in active treatment; 38% cessation in no-treatment control)⁸⁰.

The only other study to use the internet for adolescent smoking cessation was performed by Patten et al.⁸¹. This study compared the use of a home-based internet treatment, called

Stomp Out Smokes (SOS) to a brief clinic-based intervention, called the Brief Office Intervention (BOI). Participants in the SOS group achieved greater reductions in days of smoking, when compared to the BOI group (SOS reduction: 14.7 ± 30.8 ; BOI 3.4 ± 15.6), but 30-day abstinence rates at week 24 (SOS: 6%, BOI: 12%) and week 36 follow-ups (SOS: 6%, BOI: 13%) revealed no significant group differences. In addition, the majority of participants in the SOS group appeared to stop accessing the SOS website after Week 3⁸¹. Table 3 (below) summarizes the outcome data from investigations of psychosocial treatments for smoking cessation in adolescents.

Discussion

While significant progress has been made in establishing the efficacy of various treatments for adolescent smoking cessation, much work is left to be done. It is a positive step, however, to be able to draw limited conclusions about the efficacy of pharmacological treatments. This was not possible even three years ago, which points to the progress made in testing NRT and bupropion for adolescents attempting to quit smoking. Future investigations need to include newer medications, including varenicline, including further investigations of NRT and bupropion.

While statistically significant reductions in smoking have been found in studies of NRT in adolescents, it currently appears that NRT used alone is not sufficient to result in significant abstinence rates. NRT trials indicate that it is efficacious when used in combination with validated behavioral treatments; indeed, the two studies with the highest cessation rates combined NRT with CBT and/or CM. These trials had cessation rates similar to those found in the adult literature²⁶. Continued investigations of NRT with efficacious behavioral programs should be conducted, particularly to establish the optimum dosage and length of treatment with NRT. Some adolescent smokers have nicotine dependence symptoms^{82–84}, and these individuals may need NRT at higher doses and/or for longer periods than smokers without dependence symptoms⁸⁵. After examining the limited evidence available, however, NRT only appears to have modest efficacy. Thus, it may be that “nicotine replacement therapy is not a primary therapy for adolescent smoking cessation”^{86, p. 206}.

As with NRT, there have been mixed findings in investigations of bupropion. For NRT, it may be that higher doses are necessary to achieve cessation; for bupropion, this appears to be the case. While significant reductions in smoking have been found at 150 mg³⁸, one study did not find that 150 mg was effective when combined with NRT⁴¹. Poor medication adherence likely explains part of these findings, however. Other investigations^{37, 39} have used a 300 mg dose (the standard dose in adults) with modest success, especially compared to the cessation rates seen in adults²⁷. Until the study by Muramoto et al.³⁹, investigations of bupropion were performed using small sample sizes, which limited conclusions. Our research group is conducting a trial with 300 mg of bupropion for adolescent and young adult smokers; further investigations, such as this one, are needed to replicate the findings of Muramoto and collaborators³⁹ and determine the efficacy of bupropion. Overall, bupropion may have advantages over NRT in preventing weight gain commonly experienced by individuals attempting cessation⁸⁷, but cessation rates with bupropion do not appear higher at this time.

Psychosocial treatments have made much progress over the past five years, with two programs recognized for their efficacy: Project EX and the NOT program⁴⁴. Each has demonstrated efficacy in different settings and with different populations, which bodes well for their generalizability. That said, NOT has produced inconsistent results across studies, and it does not seem more effective than brief advice in males. Females, however, do appear to benefit from the NOT intervention, except for the notable case of Native American females. Project EX appears to be more consistently effective, but the school-as-community component does not seem to increase cessation rates above that of Project EX itself.

CM has been investigated only in pilot studies, but these studies have given indications of its short-term effectiveness. Critics of CM argue that it may decrease internal motivation to achieve cessation, given the patient's dependence on external reinforcement. In addition, there are ethical concerns about paying individuals to do something that they "should" be doing. Critics somewhat rightfully note that ex- and non-smokers are not paid for remaining abstinent. While a discussion of these points is outside the scope of this review, Donatelle and collaborators⁵⁵ appropriately note that it may be a choice between paying less now to foster cessation or paying more later to treat a host of smoking-related diseases. Regardless of the moral dilemmas, CM has only shown efficacy in small studies without long-term follow-up; studies with larger sample sizes and longer follow-up assessments are needed to truly establish the efficacy and potential maintenance of CM's treatment effects.

Interestingly, SMART, a teen workplace intervention, and MI have not shown consistent efficacy. Despite the lack of a significant treatment effect for either intervention, it should be noted that the contact time in each is substantially lower than in most other psychosocial interventions and that many participants in these studies were not seeking cessation treatment. Nonetheless, the lack of findings with MI is surprising in light of the conclusion made by Sussman²⁵ that MI was associated with one of the highest cessation rates; this can likely be explained by noting that those studies usually included other efficacious interventions, such as CBT. Despite the low cessation rates associated with MI, its advantages, which include low cost and ease of implementation in emergency departments or other medical settings, argue for its use in certain settings.

Finally, telephone- and internet-based interventions are in the earliest stages of development and testing. Telephone-based smoking cessation has been better studied in adults, with evidence of usefulness. In the one reported telephone-based study in adolescents, the results were not promising. It is important to reiterate the conclusions of Lipkus et al.⁷⁶, who urged further investigation of telephone treatments, especially given the adult findings. Four studies have examined the utility of the internet^{54, 79, 80, 88}, with mixed results. In all, it appears that internet-based interventions may function best as adjunctive interventions used in tandem with more intensive behavioral and/or pharmacological treatments. Nonetheless, more research is needed to evaluate internet interventions to develop the most efficacious treatment packaging (e.g., in chat rooms, one-on-one interventions, information only, etc.) and treatment orientation (e.g., CBT, MI, etc.) for internet interventions.

Limitations of the Current Literature

While the literature on adolescent smoking cessation is limited by a general lack of published studies, this is especially true for pharmacological treatments. Only seven published studies of NRT or bupropion use exist, and three of these have been open-label studies. This limits the conclusions that can be drawn. Specifically for bupropion, the lack of long-term efficacy data and the small sample sizes in the studies performed limit interpretation. In addition, the results of Muramoto and collaborators³⁹ need to be replicated to establish that 300 mg is the most effective dose of bupropion for youngsters. The study conducted by Killen and colleagues⁴¹ points towards another limitation of the literature: only one study of combined NRT and bupropion exists in the literature. While the results of the study were not significant, this should not discourage further exploration of combination treatment, as there is evidence that participants who were adherent to bupropion had a greater chance of achieving abstinence.

For psychosocial treatments, the clearest limitations are methodological. Many psychosocial treatment studies used single-group designs, did not control for contact time, and/or did not biochemically verify smoking status. NOT, for instance, compared 500 minutes of treatment to 20 minutes of brief advice. Thus, the effects seen for NOT could be an artifact of contact time, not of treatment. As seen in this example, even the best investigations often included methodological deficits. Until these design problems are remedied, it remains difficult to draw conclusions from the body of psychosocial treatment literature.

In addition, there is little evidence to tell what components of the larger theoretically-based psychosocial treatments are effective. While it can be said that cognitive-behavioral interventions aid cessation attempts²³, what it is about this treatment philosophy that fosters change cannot be stated. Cognitive-behavioral treatments are often heterogeneous interventions combining various modules (e.g., assertiveness training, relapse prevention, replacement behaviors, etc.); while some or all of these modules may be effective, it is impossible to tell which components are effective and which combinations maximize effectiveness. Finally, many of the studies examined here were comprised predominately of Caucasian samples, which limits generalizability. This is unfortunate, as smoking rates in adolescents are high across ethnic groups, although some differences in adolescent cigarette use by ethnicity have been found CDC,⁸⁹; future studies must include more individuals of non-white ethnicity to identify more specific treatments for the different subgroups of adolescents. Despite these limitations, though, the conclusion of Sussman (2002) is still valid; psychosocial treatment is associated with at least twice the cessation rate of control treatments.

Future Directions

It is unfortunate (if understandable) that much of the research in adolescent smoking cessation has evolved along two important, but separate, lines. To date, research has focused on either pharmacological or psychosocial treatment evaluation, which will eventually limit progress. The long-term goal must be to integrate both types of intervention, a concept supported by best practice guidelines for adolescent smoking cessation treatment⁹⁰. In the meantime, these two separate areas of research must be refined and expanded. First, dose

and duration of pharmacological treatments need to be further investigated. It appears that each treatment offers a somewhat effective option for cessation, but cessation rates using NRT or bupropion are still generally below 20% at follow-up. Once the optimal pharmacological treatment is elucidated, it should be combined with the optimal psychosocial treatment to maximize treatment efficacy. While this is an undertaking that could take decades, current cessation rates are low enough to justify such an investigation.

That said, simultaneous cost-effectiveness studies are warranted to establish whether fully integrated treatments are necessary for all individuals or only for those with significant symptoms of nicotine dependence. In addition, maintenance treatments need to be explored and established to prevent the post-treatment relapse of smokers, which is a common phenomenon^{30, 39}. For adults, bupropion has shown efficacy in preventing or delaying relapse to smoking^{91, 92}, but this has not been explored in adolescents. It is likely that treatments for smokers, like those for other addictive disorders and chronic medical and psychiatric conditions, will need to include continuation and maintenance phases to solidify abstinence beyond the acute treatment period. Given the immense morbidity, mortality and cost associated with smoking, investigations to establish the most cost-effective and efficacious treatments for individual adolescents, based on salient variables, should be the long-term goal for adolescent smoking cessation treatment.

Acknowledgments

This work was supported in part by grants from the National Institutes of Health (DA07238, DA14037, DA15131, DA17804, DA17805, MH62464 and MH68391), and the Sarah M. and Charles E. Seay Endowed Chair in Child Psychiatry at UT Southwestern Medical Center.

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Key Learning Objectives

1. Readers will learn about the strengths and weaknesses of pharmacological interventions for adolescent smoking cessation.
2. Readers will learn about the strengths and weaknesses of behavioral therapies for adolescent smoking cessation.
3. Readers will learn about the gaps in the current understanding of interventions for adolescent smoking cessation, and readers will learn about future directions for research in this arena.

Future Research Directions

1. Investigation of pharmacological agents to maximize the potential effects of nicotine replacement and bupropion, and an initial investigation to evaluate the safety and efficacy of varenicline in adolescent smokers.
2. Continued evaluation of developed behavioral therapies, especially cognitive-behavioral or skill-based therapies, to establish optimal treatment length and which skills are most important in promoting cessation.
3. Further investigations into promising behavioral therapies, including contingency management, that have not been fully validated and further trials involving telephone and internet-based therapies to increase treatment availability.
4. Investigations need to occur that evaluate combinations of the most efficacious pharmacological and behavioral interventions.

Adolescent Pharmacological Smoking Cessation Studies

Table 1

	Study	Design	Treatment	Adjunctive Treatment	Biochemical Abstinence	n	% White	Baseline CPD	End of Tx Cessation Rate	Follow-up Cessation Rate
NRT	Smith et al., 1996 [29]	NR, Open-label	8 weeks	Individual & group counseling	CO < 9 ppm	22	100%	23.3 ± 5.0	13.6%	4.5% (at both 3 & 6 mos.)
	Hurt et al., 2000 [30]	NR, Open-label	6 weeks	“Minimal”	CO < 8 ppm	101	95.0%	20 (median)	10.9%	4.5% (at both 3 & 6 mos.)
	Hanson et al., 2003 [31]	Double-blind, Randomized, PC	11 weeks	CBT & CM	CO < 6 ppm	100	86.9%	16.3 ± 4.9	28% vs. 24% (placebo)	No data
	Moolchan et al., 2005 [35]	Double-blind, Randomized, PC	12 weeks	CBT	CO < 7 ppm	120	72.5%	18.8 ± 8.6	20.6% (patch) vs. 5% (placebo) 8.7% (gum) vs. 5% (placebo)	20.6% (3 mo.; patch) vs. 5% (placebo) 8.7% (3 mo.; gum) vs. 5% (placebo)
Bupropion	Upadhyaya et al., 2004 [37]	NR, Open-label	7 weeks	2 “brief” sessions	CO < 8 ppm	16	88%	18.06	31.3% (after 4 weeks) *	No data
	Niederhofer & Huber, 2004 [38]	Double-blind, Randomized, PC	90 days	“Behavioral treatment”	CO, ppm not given	22	No data	<10	54.5% vs. 18.1% (placebo)	No data
Both	Killen et al., 2004 [41]	Double-blind, Randomized, PC (bupropion only)	8/9 weeks **	Group Skills Training	CO < 9 ppm	211	50.2%	15.39	28% (NRT + placebo) 23% (NRT + bupropion)	7% (26 wks.; NRT + placebo) 8% (26 wks.; NRT + bupropion)

CBT = Cognitive-Behavioral Therapy

CM = Contingency Management

CO = Carbon Monoxide

CPD = Cigarettes per Day

Mos. = Months

NR = Non-randomized

NRT = Nicotine Replacement Therapy

PC = Placebo-controlled

* = While treatment was for 7 weeks, data were only presented for 4 weeks of treatment

** = 8 weeks for NRT, 9 for bupropion

Table 2

Design Characteristics of Adolescent Behavioral Smoking Cessation Studies

Study	Treatment Used	Length	Control Group	Biochemical Abstinence
EX	Sussman et al., 2001 [45]	8 sessions, 6 wks.	“Standard Care”	CO < 9 ppm
	Zheng et al., 2004 [48]	8 sessions, 6 wks.	None	SC, cutoff not given
NOT	Dino, Horn, Goldcamp, Fernandes et al., 2001 [50]	10 weekly 50-min. sessions	10 min. BA	CO < 9 ppm
	Dino, Horn, Goldcamp, Maniar et al., 2001 [51]			
	Horn, Dino, Kalsekar, & Fernandes, 2004 [52]			
	Horn et al., 2005 [53]			
CM	Roll, 2005 [32]	4 wks.	BA	CO < 6 ppm
	Krishnan-Sarin et al., 2006 [33]	4 weekly sessions	CBT only	SC, semi-quantitative
MI	Brown et al., 2003 [64]	2 45-min. sessions	10 min. BA	SC < 15ng/ml & CO < 10 ppm
	Colby et al., 2005 [65]	2 sessions, 50 min. total	5 min. BA	SC < 15ng/ml & CO < 9 ppm
	Helstrom et al., 2007 [66]	1 session, time not given	1 educational session	SC < 15ng/ml
	Stoddard et al., 2005 [60]	1 year	No treatment	None noted
	Lipkus et al., 2004 [76]	N/A	Self-help materials	SC, not used in analyses
	Woodruff et al., 2001 [79]	7 1-hour “chats”	None	None noted
	Woodruff et al., 2007 [80]			
	Patten et al., 2006 [81]	24 weeks of access to website	4-session brief intervention	CO < 9 ppm

BA = Brief Advice

CBT = Cognitive-Behavioral Therapy

CM = Contingency Management

CO = Carbon Monoxide

MI = Motivational Interviewing

SAC = School as a Community Intervention

SC = salivary cotinine

Table 3

Outcome Data from Adolescent Behavioral Smoking Cessation Studies

	Study	n	% White	Baseline Cigarettes per Day	End of Tx Cessation	Follow-up Cessation
EX	Sussman et al., 2001 [45]	259	27%	8.8 ± 9.3	14% (control was not given)	30%/17%* (3 mo.) vs. 16%/8%* (control)
	Zheng et al., 2004 [48]	46	0% (all Chinese)	5.7	12.4% (7-day continuous); 3.8% (30-day continuous)	14.3% (7-day continuous); 10.5% (30-day continuous)
NOT	Dino, Horn, Goldcamp, Fernandes et al., 2001 [50]	566	81.3%	13.1 ± 8.0	No data	21.7% (7.3 mo.) vs. 12.6% (control)
	Dino, Horn, Goldcamp, Maniar et al., 2001 [51]	346	87.3%	13.1 ± 8.0	17.3% (3 mo.) vs. 11.3% (control)	19.4% (5.5 mo.) vs. 11.7% (control)
	Horn, Dino, Kalsekar, & Fernandes, 2004 [52]	258	93%	13.2	8.1% (3 mo.) vs. 2.2% (control)	8.1% (6 mo.) vs. 4.5% (control); 10.5% (15 mo.) vs. 8.2% (control)
	Horn et al., 2005 [53]	74	< 17.8% (not given)	8.8 ± 12.3	11.1% (3 mo.) vs. 5% (control)	No data
CM	Roll, 2005 [32]	22	68.2%	No information	50% vs. 10% (control)	66% (1 mo.) vs. 40% (control)
	Krishnan-Sarin et al., 2006 [33]	28	Not given	No information	53% vs. 0% (control)	No data
MI	Brown et al., 2003 [64]	191	94.8%	14.5 ± 9.4	No data	11% (1 mo.) vs. 11% (control); 13.3% (6 mo.) vs. 8.5% (control); 14.4% (1 yr.) vs. 9.9% (control)
	Colby et al., 2005 [65]	85	55%	10.5 ± 7.3	No data	2% (1 mo.) vs. 0% (control); 5% (3 mo.) vs. 0% (control); 9% (6 mo.) vs. 2% (control)
	Helstrom et al., 2007 [66]	81	79%	11.2 ± 8.46	No data	5.2% (1 mo.) vs. 6.8% (control); 9.5% (6 mo.) vs. 7.4% (control)
	Stoddard et al., 2005 [60]	322	66.9%	Not given	8.9% vs. 2.2% (control)**	No data
	Lipkus et al., 2004 [76]	402	82%	10 ± 8	No data	16% (4 mo.) vs. 11% (control); 21% (8 mo.) vs. 19% (control)
	Woodruff et al., 2001 [79]	26	55%	4.4 ± 3.2	22% (no control)	33.3% (1 mo.; no control)
	Woodruff et al., 2007 [80]	136	28%		35% vs. 22% (control)	39% (3 mo.) vs. 47% (control); 37% (1 yr.) vs. 38% (control)
	Patten et al., 2006 [81]	139	88%	9.8 ± 5.9	6% vs. 12% (control)	6% vs. 13% (control)

* = all lost to follow-up assumed to continue smoking and rate adjusted for biochemical verification

** = data not specifically listed; extrapolated from Table 2 of the original citation