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Journal

Clinical Psychological Science, 1(4)

ISSN

2167-7026

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Publication Date

2013-10-01

DOI

10.1177/2167702613484717

Peer reviewed

Published in final edited form as:
Clin Psychol Sci. 2013 October ; 1(4): 401–412. doi:10.1177/2167702613484717.

A Mood Management Intervention in an Internet Stop Smoking Randomized Controlled Trial Does Not Prevent Depression: A Cautionary Tale

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Abstract

Smoking and depression are related, and mood management interventions included in smoking cessation interventions can increase smoking abstinence rates. Could a mood management intervention embedded in an Internet-based smoking cessation intervention prevent major depressive episodes? Spanish- and English-speaking smokers (N = 17,430) from 191 countries were randomized to one of four online self-help intervention conditions (two with mood management). We analyzed preventive effects among those participants without a major depressive episode at baseline. The mood management intervention did not reduce the incidence of major depressive episodes in the following 12 months. However, we found a mood management by depression risk interaction (OR = 1.77, p = .004), such that high-risk participants who received the mood management intervention had an increased occurrence of major depressive episodes (32.8% vs. 26.6%), but not low-risk participants (11.6% vs. 10.8%). Further research on whether mood management interventions may have deleterious effects on subsets of smokers appears warranted.

Keywords

prevention of depression; Internet intervention; depression; smoking cessation; prevention

Tobacco use is the number one cause of preventable death in the world (World Health Organization [WHO], 2011) and is estimated to cause one billion deaths in the 21st century if current smoking rates continue (WHO, 2011, 2012). Depression is the number one cause

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Declaration of Conflicting Interests
The authors declared that they had no conflicts of interest with respect to their authorship or the publication of this article.

of disability worldwide (Moussavi et al., 2007) and is implicated in many health problems, including smoking (Hall, Muñoz, Reus, & Sees, 1993; Hall & Prochaska, 2009). In addition to research that focuses on these problems individually, studies that examine the interaction of these problems and their treatment, both individually and combined, will help advance clinical science. The massive impact of both of these conditions on the global burden of disease demands continued progress in preventing and treating them, with a major focus on effective interventions that are highly scalable.

In response to the above challenges, our research program has addressed both depression and smoking singly and in combination. We have conducted smoking cessation clinical trials showing that mood management interventions can increase abstinence rates when administered in traditional face-to-face treatment trials with English speakers (Hall et al., 1996; Hall, Muñoz, & Reus, 1994), as well as via print and audio recording media sent to Spanish-speaking smokers via surface mail (Muñoz, Marín, Posner, & Pérez-Stable, 1997). The mood management intervention draws on another of our research programs, namely a series of studies testing whether cognitive behavioral self-management methods can be used successfully to treat major depression. We found that treatments designed to train depressed individuals solely on (a) increasing pleasant activities (now called “behavioral activation”; Dimidjian, Barrera, Martell, Muñoz, & Lewinsohn, 2011), (b) interpersonal skills training, or (c) cognitive training, were significantly better at reducing depressive symptoms when compared to a waiting list control, but not significantly different from each other (Zeiss, Lewinsohn, & Muñoz, 1979). The single-focus treatment protocols used in that study were published as a self-help book (Lewinsohn, Muñoz, Youngren, & Zeiss, 1978) and used as the basis of a series of treatment manuals developed and tested at San Francisco General Hospital and elsewhere (Cuijpers, Muñoz, Clarke, & Lewinsohn, 2009; Muñoz & Mendelson, 2005). These manuals were adapted to be used as the mood management intervention in the smoking trials mentioned above.

One of our major goals has been to move beyond treatment and determine whether major depressive episodes can be prevented. We conducted the first randomized controlled depression prevention trial in the early 1980s (Muñoz et al., 1995; Muñoz & Ying, 1993; Muñoz, Ying, Armas, Chan, & Gurza, 1987), developed interventions for the prevention of postpartum depression (Le, Zmuda, Perry, & Muñoz, 2010; Muñoz et al., 2007; Tandon, Perry, Mendelson, Kemp, & Leis, 2011), and have reviewed the prevention of depression field throughout the years (Muñoz, Cuijpers, Smit, Barrera, & Leykin, 2010; Muñoz, Le, Clarke, Barrera, & Torres, 2008), finally being able to assert that, indeed, major depression can be prevented (Muñoz, Beardslee, & Leykin, 2012). Several lessons were learned in this process. First, prevention trials by definition need to ascertain that individuals in the trial are not already depressed, that is, they are not yet “cases” and they do not meet diagnostic criteria for major depressive episode (MDE) upon entry. The key test for preventive effects is the comparative incidence rates between the experimental and control conditions. Specifically, the proportion of individuals who meet criteria for MDEs (i.e., become “cases”) during the trial period in the experimental condition should be significantly lower than that for the control group. Second, most people do not become depressed. When the incidence is very low, impractically large sample sizes are needed to detect even lower incidence rates. Thus, to carry out prevention trials with realistic sample sizes, it is crucial to

identify subgroups at imminent high risk for depression, that is, individuals who are likely to develop an MDE within the following year, rather than at some point in their lifetime. This is likely why trials of universal prevention programs tend to have little support for their ability to reduce incidence (Sheffield et al., 2006; Spence, Sheffield, & Donovan, 2003). Instead, indicated or selected prevention programs targeted to higher-risk populations hold greater promise (see Muñoz et al., 2010). Our work identifying pregnant women at risk was useful in constructing a high-risk algorithm, showing that a history of MDEs and/or high symptoms of depression in people who do not meet criteria for MDE according to the *Diagnostic and Statistical Manual of Mental Disorders* (*DSM*; American Psychiatric Association, 2000) can have incidence rates of 25% or higher, rather than the general population risk of 1% to 2% per year (Kessler et al., 1994). Last, cognitive-behavioral interventions are effective at substantially reducing this risk among at-risk samples (Cuijpers, van Straten, Smit, Mihalopoulos, & Beekman, 2008), and the preponderance of the evidence is that this can be done in many populations (Muñoz et al., 2010).

These studies and our desire to expand the reach of health services led to our launching a smoking cessation research Web site (http://stopsmoking.ucsf.edu and http://dejardefumar.ucsf.edu). The Internet is a powerful tool to advance the public's health by providing access to accurate information about health issues of concern. Furthermore, the Internet can house culturally and age-appropriate interventions. The smoking cessation content for the research Web site was adapted from a self-help guide developed for a community-based intervention in Latinos (Muñoz et al., 1997) and updated and strengthened with a guide of pharmacological interventions. Our site has been shown to yield abstinence rates of about 20% that are comparable to those of commonly used smoking cessation interventions such as the nicotine patch and smoking cessation groups (Muñoz, Aguilera, Schueller, Leykin, & Pérez-Stable, 2012; Muñoz et al., 2006; Muñoz et al., 2009).

In addition to our smoking site, effective Internet interventions have been developed for various mental health issues such as depression and anxiety (Calear, Christensen, Mackinnon, Griffith, & O'Kearney, 2009; Spek et al., 2007). These sites offer low-cost and widely accessible treatment options. Internet interventions might be especially valuable for prevention where the emphasis on a population approach to public health demands low-cost, efficacious interventions with high levels of reach and access (Christensen & Griffiths, 2002; Muñoz, Beardslee, et al., 2012). Indeed, Internet interventions are highly scalable, can include very large international samples, and, because of these large sample sizes, provide sufficient statistical power to test preventive effects as well as secondary hypotheses. For example, we found that in our smoking site, smokers who achieved abstinence did not report higher levels of depression (Torres et al., 2010). We also found that individuals are able to choose the most appropriate tools from the menu available on our site given their personal characteristics and as a result improve their outcome. In a participant preference trial, individuals meeting criteria for MDEs were significantly more likely to pick a mood management course (82.1% vs. 75.2%), and those who did so were more likely to report 7-day quit rates than those who did not (37.2% vs. 22.2%; Schueller, Leykin, Pérez-Stable, & Muñoz, 2013).

One of the practical issues in conducting prevention campaigns is that individuals may not know that they are at higher risk, and thus may not have the motivation to seek preventive interventions. It occurred to us, then, that our smoking cessation Internet trials provided an opportunity to examine the preventive effects of a mood management intervention in people who were at high risk (using the risk algorithm described above) but who had not sought information or an intervention focused on depression. Our randomized controlled trials consisted of four conditions, two of which included an eight-session online mood management intervention and two of which did not. Moreover, we obtained self-reports of the symptoms required to screen for an MDE at baseline and at 1-, 3-, 6-, and 12-month follow-ups. This allows us to determine (a) if our high-risk algorithm predicted higher annual incidence of MDEs and (b) whether smokers screening negative for MDEs at baseline and randomly assigned to receive a mood management intervention as part of a stop smoking Internet site would have lower annual incidence of MDEs than those randomized to other conditions.

Method

Participants and procedure

Participants were drawn from the sample of 17,430 smokers from 191 countries who participated in an Internet-based smoking cessation intervention between November 2005 and September 2009. This includes two nearly identical trials whose study procedures are described in more detail elsewhere (Leykin, Aguilera, Torres, Pérez-Stable, & Muñoz, 2012; Muñoz et al., 2009). Both trials underwent institutional review board evaluation and received approval at all relevant institutions. The first trial included the first 1,000 consented participants, who received follow-up assessment phone calls from a research assistant if they failed to provide data after receiving automated e-mail reminders. The rest did not receive such follow-up phone calls. Due to these procedures to maintain the cohort, we refer to this initial sample as the “cohort maintenance” sample and the subsequent group as the “recruitment” sample. The cohort maintenance sample was stratified by language so that half of the participants used the Spanish site. The intervention and online experience, however, were identical for both trials. For the current investigation, as we were interested in the prevention of depression, that is, the effect on incidence (the proportion of new cases), we excluded those who met criteria for an MDE at baseline according to a mood screener questionnaire, thus reducing the sample for analysis to 14,483 smokers (866 from the first 1,000 and 13,617 from the subsequent 16,430).

Eligibility criteria included being 18 years of age or older, smoking five or more cigarettes per day, having regular access to e-mail and the Internet, and intending to quit within the next month. Following their initial visit, participants were required to return three times in 7 days to report the number of cigarettes smoked. Those who met this requirement were randomized to one of four conditions, given access to the intervention Web site, and sent automated follow-up assessment emails at 1, 3, 6, and 12 months after their quit date. Both English and Spanish versions of the Web site were available to participants.

Intervention

The intervention consists of nine components; one of these is an eight-lesson cognitive-behavioral mood management self-help course that teaches how thoughts, activities, and people relate to one's mood and how promoting helpful thoughts, pleasant activities, and positive interpersonal interactions can help participants gain control of their mood. The principles of this module are based on the widely studied Coping With Depression course, which has been found to be an effective self-help resource for both the treatment and prevention of depression (Cuijpers et al., 2009). Participants were assigned to one of four conditions that build cumulatively. The most basic condition contained a smoking cessation guide, cigarette counter, and online journal. Condition 2 added individually timed e-mail messages. Condition 3 added the mood management course described in the introduction. Condition 4 added an asynchronous bulletin board that allowed communication among study participants in this condition. Thus, both Condition 3 and Condition 4 contained the mood management course. Figure 1 displays the flow of participants through the site.

Measures

Depressive episodes—The MDE Screener (Muñoz, 1998) is a self-report measure of the nine symptoms of MDEs and impairment in functioning and was the main outcome in this analysis. Participants completed this measure for current and lifetime symptoms of depression at baseline and for current symptoms at each follow-up. Participants were considered to screen positive for an MDE if they endorsed five of the nine symptoms (with one being depressed mood and/or anhedonia) and an item reflecting impairment in functioning. This is consistent with the *DSM-IV* criteria for an MDE and the principal outcome in this analysis. Although self-report is not equivalent to a clinical diagnosis, this self-report measure shows high concordance with a well-validated screener for depression (PRIME-MD; Muñoz, McQuaid, Gonzalez, Dimas, & Rosales, 1999) and with clinician-administered measures with a sensitivity of .969 and specificity of .967 (Vázquez, Muñoz, Blanco, & López, 2008). Life history of depressive episodes (the same criteria for an MDE applied to lifetime symptoms) was used as one of two indicators of defining the higher risk group.

Depressive symptoms—The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) is a 20-item self-report scale that measures current level of depressive symptoms. Scores of 16 or greater were considered significant depressive symptoms and used as the second indicator to define the higher risk group (Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977).

Web site utilization—As participants used the Web site, various metrics of participation were captured, allowing us to infer the degree to which participants received and interacted with the site content. For example, the Web site logged the last lesson that the participant had viewed in its entirety (progressed through all the screens) as well as the use of any of the Web-based tools (e.g., mood, activity, thought trackers; relaxation tool). These variables were used in analyses to investigate the relationship between interacting with the site and incidence of MDEs.

Statistical analysis

For the current investigation we made use of available data to analyze the effects of the mood management tools on subsequent incidence of depressive episodes. Smoking abstinence outcomes were previously reported (Leykin et al., 2012; Muñoz et el., 2009). First, we analyzed baseline characteristics of each sample (cohort maintenance and recruitment). We then conducted mixed-effects logistic regressions with depression status as the outcome, including age, gender, ethnicity, language, education, income, employment, and number of cigarettes smoked as covariates. As occurrence of MDEs is a low base-rate observation in the general population, most studies of prevention select high-risk samples to have the statistical power necessary to observe a preventive effect (see Muñoz et al., 2010). In this study, we retained all visitors to the Web site not meeting criteria for MDE at baseline but defined a high-risk group as those with elevated self-reports of depressive symptoms (CES-D ≥ 16 at baseline), life history of MDEs, or both, an algorithm that successfully predicted higher incidence in earlier studies (Le, Muñoz, Soto, Delucchi, & Ghosh Ippen, 2004; Muñoz et al., 2007). Risk for depression was included as a predictor in the mixed-effects logistic regression. After conducting the mixed-effects model, we examined occurrence of MDEs at any time point among those who received mood management versus those who did not receive mood management separately for the low-risk and high-risk groups using chi-square difference tests. Further logistic regressions assessed whether predictors such as completion of lesson content or use of online tools from the mood management lessons were related to higher rates of depressive episodes.

Results

Sample characteristics

We first tested differences across the samples to see if those who were recruited into the cohort maintenance sample differed from those in the recruitment sample in such a way that might bias the results. Table 1 displays participant characteristics by sample separated by those who were randomly assigned to either the mood management or no mood management group. As designed, the proportion of English and Spanish speakers was balanced in the cohort maintenance sample but not in the recruitment sample. We also observed higher rates of MDEs at follow-up in the cohort maintenance sample than the recruitment sample, suggesting that participants with new MDEs at follow-up may have been less likely to complete online follow-ups on their own. Other differences between the samples, even when significant, were quite minor. For example, the recruitment sample was slightly more likely to be employed and reported less history of depression than the cohort maintenance sample. The cohort maintenance sample was significantly older (M = 37.90 years, SD = 20.92 vs. M = 36.58 years, SD = 12.00) and reported more education than the recruitment sample. Given minor differences on most measures and because the experiences of the samples were identical (except that those in the cohort maintenance sample were called if they did not respond to initial e-mail reminders for follow-ups), we combined these samples for subsequent analyses.

Predicting MDE

We hypothesized that participants who received the mood management module would be less likely to experience subsequent episodes of depression. We conducted a mixed-effects logistic regression predicting MDEs at each time point controlling for baseline depressive symptoms as measured by the CES-D, number of cigarettes smoked, and demographic variables (age, gender, ethnicity, language, education, employment, and income) and including risk status (low risk vs. high risk), assignment to mood management, and the risk status by mood management interaction as predictors. Our risk assessment algorithm significantly predicted 1-year incidence of MDEs: The incidence for the high-risk group was 29.6%, and the incidence for the low-risk group was 11.2% (*OR* = 1.55, $p = .01$, 95% CI, 1.15–1.76). Assignment to mood management was not a significant predictor of incidence of MDEs (*OR* = 1.01, $p = .94$, 95% CI, 0.78–1.32); however, there was a significant risk status by mood management interaction (*OR* = 1.77, $p = .004$, 95% CI, 1.20–2.59). The only covariates that predicted subsequent MDEs were depressive symptoms (*OR* = 1.22, $p < .001$, 95% CI, 1.21–1.24) and number of cigarettes smoked (*OR* = 1.02, $p = .001$, 95% CI, 1.01–1.03). To better understand the nature of the interaction, we looked at the percentage of those who experienced a depressive episode during at least one follow-up assessment. We first considered the high-risk group, as its members would more likely demonstrate a preventive effect if it exists. Of those who received the mood management module, 32.8% reported experiencing a depressive episode compared with 26.6% of those who did not receive mood management ($p = .001$, $\Phi = .07$). We then examined differences within the low-risk group; 11.6% of those receiving the mood management module reported a depressive episode compared with 10.8% of those who did not receive mood management (n.s., $p = .42$, $\Phi = .01$). These analyses suggest that receiving the mood management intervention was associated with increased reports of MDEs during the follow-up period for those at high risk for depression but not for participants who were at low risk.

Attrition and usage

We next repeated these analyses separately for the cohort maintenance sample (which had higher response rates) and the recruitment sample to see if the link between receiving the mood management module and increased reports of MDEs among participants at high risk for depression would replicate across samples. We completed these analyses because we were concerned that the high attrition rates might bias the results and replication across samples would strengthen our confidence in the conclusions. Of participants in the cohort maintenance sample, 82.7% (716 of 866) completed at least one follow-up assessment. For the recruitment sample, even with the lack of phone follow-ups, 48.4% (6,595 of 13,617) of participants provided data during at least one follow-up assessment. For high-risk participants, the difference between mood management and no mood management was not significant in the cohort maintenance sample ($p = .54$), but the size and the direction of the effect were similar to those of the recruitment sample (see Table 2). Thus, the difference in significance is likely due to size of the sample and not bias introduced due to differences in the attrition rates across the samples. In the low-risk group a similar pattern was found with similar effect sizes and patterns across the samples yet nonsignificant differences across participants receiving and not receiving the mood management module.

We then looked at predictors of attrition to determine if baseline predictors or assignment to different conditions were linked to higher attrition rates and thus might bias the results. Baseline CES-D scores, life history of MDE, and baseline MDE did not predict who would drop out, looking at the combined low-risk and high-risk groups and at each group separately. Furthermore, attrition rates from follow-up did not differ across the conditions. This reinforces confidence in the findings despite the higher rates of attrition and suggests that individuals with higher depressive symptoms were not more likely to continue to complete follow-up assessments if given mood management and thus inflate subsequent reports of MDE.

Last, to strengthen confidence that the mood management module was linked to increased risk of MDEs, we investigated whether those who interacted with the site more reported greater rates of MDE. Given that only high-risk participants experienced increased risk of MDEs, we restricted these analyses to these participants. We conducted logistic regressions (n = 1,314) predicting depression at follow-ups from the last lesson the Web site recorded a participant viewed, controlling for initial levels of depressive symptoms. Last lesson viewed predicted MDE at follow-up (OR = 1.06, p = .02, 95% CI, 1.01–1.12). We also sought to disentangle the relationship between progressing further through the content and depression as it might be that those with higher initial levels of depression were more likely to use the Web site, thus confounding our findings. None of the baseline indicators of depression correlated highly with progressing further in the mood management course (CES-D, r = −.05; lifetime MDE, r = −.02; baseline MDE, r = −.06), suggesting that those identified as more depressed did not tend to view more lessons. Last, usage of the Web-based mood management tools predicted higher rates of MDE at follow-ups (OR = 1.004, p = .015, 95% CI, 1.001–1.006). Although this odds ratio may appear small, it is worth noting that tool use is a continuous variable (number of times a participant used a tool) and many of the participants who used the tools did so quite frequently. Again, there was no relationship with usage of mood tools and baseline depression indicators (CES-D, r = −.002; lifetime MDE, r = .007; baseline MDE, r = −.017). These results suggest that progressing further through the mood management module and using the tools more actually corresponded to increased risk of MDEs.

Discussion

This study investigated whether a mood management intervention embedded in an Internet-based smoking cessation intervention could prevent the occurrence of MDEs. Our major hypothesis was not supported by our data: Randomization to conditions with a mood management intervention was not associated with lower incidence of MDEs in participants who screened negative for current MDEs at baseline. Given that our past research on depression prevention suggests the need to identify subsets at risk for depression, we conducted further analyses after classifying participants as high risk or low risk. The risk algorithm used high levels of depressive symptoms or a life history of MDEs at baseline, and this algorithm successfully predicted likelihood of developing an MDE within 12 months across the entire sample, as it had in another study with a group of pregnant women (Le et al., 2010). This secondary analysis showed that participants at high risk for depression who received mood management tools actually reported increased rates of MDEs at follow-

up. This effect was not found among lower-risk participants. Furthermore, among the participants at high risk for depression who received mood management intervention, viewing more lessons and greater usage of the lessons as indicated by metrics of Web utilization captured from the site (last lesson viewed and use of mood management Web site tools) also predicted higher rates of MDEs. This suggests the worrisome possibility that providing a mood management intervention as part of a smoking cessation intervention leads to increased incidence of MDEs among smokers at heightened risk for depression. We were surprised at these findings. Our search for similar effects yielded one other study that showed increased symptoms of depression among 179 smokers with a history of depressive disorder who received a smoking cessation treatment with or without an integrated cognitive-behavioral intervention for depression (Kahler et al., 2002). In that study incidence of depression was 15.2% and was not associated with abstinence from smoking, but those who received the cognitive-behavioral intervention had a higher incidence of depression (Kahler et al., 2002).

As these findings have interesting and intriguing clinical implications, it is important to consider them within the context of this intervention. Participants visited the site to receive an intervention to help quit smoking, not to address symptoms of depression. Furthermore, increased rates of depressive episodes occurred only among those who had indicators of risk for depression (e.g., high symptom levels or life history) but did not meet criteria for depression at baseline. Thus, the only participants who appeared to have unintended adverse effects of the intervention were smokers seeking a smoking cessation resource with subthreshold depressive symptoms or history of depressive episodes. All these participants were given feedback at baseline that their mood ratings were higher than average, and they were encouraged to seek consultation from their primary care clinician if their mood worsened. Perhaps this warning, combined with the mood management intervention for those assigned to it, resulted in increasing attention to or rumination on already elevated depressive symptoms, consequently putting such participants over the screening threshold for MDEs.

Randomly assigning those at higher risk for MDEs to a mood management intervention may thus increase incidence of such episodes by increasing attention to depressive symptoms, resulting in either increased *self-report* of depressive symptoms or increase in actual depressive symptoms. On the other hand, providing a mood management intervention as a choice appears to have positive effects. Those with MDEs were more likely to pick this element when given the choice, and those who did were more likely to quit smoking with no impact on subsequent levels of MDE (Schueller et al., 2013). Elsewhere, integrated substance abuse and mental health interventions have demonstrated efficacy (e.g., McFall et al., 2010; Watkins et al., 2011), but with clinicians providing these interventions in person within health care systems. It might be more difficult to combine such resources effectively using brief interventions delivered on a self-help Web site. Future research should use these findings to advance our scientific understanding regarding the long-sought-after goal of which interventions are most efficacious for which individuals in which contexts.

Clinical researchers are often encouraged to examine their data not only for positive effects, but also for unintended negative effects. There is clear evidence that some face-to-face

interventions may produce iatrogenic effects (Lilienfeld, 2007; Mohr, 1995). We can therefore predict that some Internet interventions may do the same. Therefore, researchers should be careful to test unexpected consequences of interventions that are intended for wide dissemination. Despite evidence suggesting that cognitive-behavioral strategies can prevent depression even when administered via self-help (Christensen, Griffiths, & Jorm, 2004; Muñoz et al., 2010), the brief mood management intervention contained within this Internet self-help smoking cessation site was not found to be effective in preventing depression. In addition, it seemed to have increased incidence of MDEs for the subset of smokers at high risk for depression. Nevertheless, it is worth reiterating that past research demonstrates that this intervention does increase quit rates (Muñoz et al., 1997), with quit rates of about 20% at 12 months (Muñoz et al., 2006; Muñoz et al., 2009). Thus, further research is needed to provide guidance to the field regarding whether the slightly increased risk of depression in a subset of smokers justifies the positive effect of this intervention element on smoking. In addition, it is worth reiterating that quitting itself is not related to increased depressive episodes in online samples (Torres et al., 2010).

These findings should be weighed considering the limitations of this study. First, we used only a self-report screening tool for MDEs. This tempers the generalizability of these findings, as reports were provided by visitors to a Web site with no live communication with or verification by a professional. Although the MDE screener showed 97% sensitivity and specificity with clinician-administered measures (Vázquez et al., 2008), this same research found a positive predictive value of .646, suggesting a slightly higher tendency to suggest individuals have MDE even if a clinician-administered measure would not find this. Thus, it is possible that our results may have been different had we used clinician-administered measures. Another possibility stemming from the use of self-report is that the mood management module increased awareness of symptoms of depressions, such that participants who viewed the lessons may have become more vigilant for these symptoms and thus noticed and reported more symptoms, even if the actual symptoms remained stable. We noted a small, yet nonsignificant, increase in incidence in the low-risk group as well, which could be attributed to increased vigilance. The mood management intervention does contain information and training in the symptoms and identification of depression. Subsequent trials could make use of additional forms of measurement, such as analog mood rating scales, to test this alternative explanation. Second, the attrition rates in this study were high, as is often the case in Internet trials. Findings may be due to biased responding, with those more likely to notice depressive symptoms because of exposure to mood management being more likely to return. It is worth noting, however, in the first sample, when cohort maintenance procedures were used and higher response rates obtained, the results were similar to the larger recruitment sample. Furthermore, on all of the measures of symptom severity at baseline, we found no differences among those who completed follow-up measures and those who did not, thus lowering the likelihood that the results are explained by selection bias of respondents. Finally, even the group in our sample of smokers labeled “lower risk” for depression still had a 1-year incidence of 11% by the MDE screener test, which is much higher than the average risk of 2%.

These results raise the possibility that interventions that have been found to reduce depressive symptoms when users are mindfully seeking to reduce such symptoms may not

be effective (in reducing symptoms) when users are seeking another objective, such as stopping smoking. Indeed, a conclusion drawn by the authors of the other study to find negative effects of a cognitive-behavioral intervention on major depression when provided to smokers was that the rationale for inclusion of cognitive-behavioral aspects in smoking interventions should be the importance of coping with negative mood to prevent future relapses rather than merely the reduction of affective disturbance following quitting (Kahler et al., 2002). We examined other studies in which cognitive-behavioral mood management methods were used in smoking cessation trials and found that, indeed, depressive symptoms did not significantly decrease in those administered the mood management interventions, even though the mood management interventions were associated with higher quit rates. For example, in a study by Hall and colleagues (1996), mood management interventions yielded significantly higher quit rates, but not significantly lower depressive scores. Tsoh et al. (2000) noted that neither mood management nor nortriptyline for the treatment of smoking cessation was related to the risk of MDEs during a series of smoking cessation trials. The Muñoz and colleagues (1997) study showed much higher quit rates for the mood management condition, but no significant differences in depressive symptoms.

These findings could be attributable to demand characteristics or participant motivation. Participants in depression trials expect their symptoms to be reduced, and may thus focus their efforts in doing so and succeed at this goal with the mood management tools. Indeed, research suggests that even interventions with demonstrated efficacy might be beneficial only to those who receive the intervention with knowledge of its purpose rather than those who receive it under different circumstances (Lyubomirsky Dickerhoof, Boehm, & Sheldon, 2011). Thus, when participants in smoking trials are focused on quitting, they might use the mood management tools to aid their quit attempt, but not to change their mood. Of course, demand characteristics could merely change self-report, rather than the mood itself, in which case we would be dealing with a problem in measurement. Changes in mood may be occurring similarly in both types of studies, but only users in depression studies report greater change because they expect to do so. This possibility could be examined more convincingly when using outcome variables that can be measured more objectively In a thought-provoking article on exercise and the placebo effect, Crum and Langer (2007) measured 84 female room attendants on physiological health variables affected by exercise. One group was told that cleaning hotel rooms was good exercise, whereas a control group was not given this information. Four weeks after intervention, the informed group not only perceived themselves to be getting significantly more exercise, but also showed decreases in weight, blood pressure, body fat, waist-to-hip ratio, and body mass index (cf. Stanforth, Steinhardt, Mackert, Stanforth, & Gloria, 2011, who could not replicate this finding).

Bandura (1977) has addressed this potential placebo effect as arising from changing people’s outcome expectations, which influences self-efficacy and the behaviors people undertake to achieve a goal. The effect of psychological interventions on self-change goals may be mediated by these outcome expectations and the conscious intention (and corresponding effort) to change according to specific goals. Changes found in the literature may be due to effects of demand characteristics on self-reports, the actual (objective) dependent variable, or both. This suggests including objective measures whenever possible.

The current design also suggests that it is possible to conduct randomized controlled trials (RCTs) with two or more simultaneous goals. In this smoking cessation RCT, we conducted stratified randomization by MDE status at baseline. This allowed us to test the effect on both smoking and depression. One could imagine a similar study on mood management in which participants are stratified by smoking status (or other substance use) and the main intervention could include embedded "habit abatement" elements that could be used to stop smoking. Because participants came explicitly to learn mood management, the main hypothesis would test for changes in mood levels, but, with this design, we could also test differences in quit rates, to see whether stop smoking methods found to be effective in smoking cessation trials also produce similar effects in trials focused on mood.

In summary, then, mood management has generally been shown to either increase or to have no detectable effect, but not to lower quit rates (Hall et al., 1994; Hall et al., 1996; Muñoz et al., 1997; Muñoz et al., 2006; Muñoz et al., 2009). Quitting does not appear to increase MDEs (Torres et al., 2010; Tsoh et al., 2000). People who are depressed are more likely to choose mood management components in a participant preference paradigm, and if they do so, they are more likely to quit (Schueller et al., 2013). Therefore, mood management tools appear to be a useful element in smoking cessation programs. But our current analysis shows that it is possible that, for a subset of smokers who are at high risk for MDEs, providing a mood management tool may push them over the threshold into an MDE. This may be related to the mode of delivery, in this case, to a self-help Internet intervention with no human support. Although Internet interventions hold great promise for expanding reach, these findings suggest closer examination regarding whether they are appropriate in complex cases, such as comorbidities or integrated treatment. In other work, the suggestion has been made that Internet interventions are beneficial for individuals with mild to moderate levels of disorders but not more severe cases (Andersson et al., 2005; Christensen, Griffiths, & Farrer, 2009; McKendree-Smith, Floyd, & Scogin, 2003). Further research should examine whether this increase in incidence of MDEs in smokers at high risk for them is replicable, and, if so, make this effect known to health care providers and to smokers themselves. Additional findings of unintended negative effects, especially in Internet interventions, might lead to the recommendation to remove certain intervention elements in some cases to better tailor approaches for given populations or individual users.

Acknowledgments

We would also like to thank the Center for Health and Community at UCSF, the Information Services Unit, Leslie Lenert, Carlos Penilla, Eduardo Ballesteros, and Thomas Manley for their contributions to this line of research.

Funding

This research program was supported by the Tobacco Related Disease Research Program, the University of California, Office of the President, the Google Adwords Grants Program, and the Brin/Wojcicki Foundation (Muñoz, PI), the Tobacco Research Network Program, Fogarty International Center, National Institute on Drug Abuse, National Institutes of Health, USA (Grant Number TW05935), the National Cancer Institute for Redes en Acción (U01CA86117 and U54CA153511, Pérez-Stable, co-PI), and NIMH Grant F32MH095345 (Schueller, PI).

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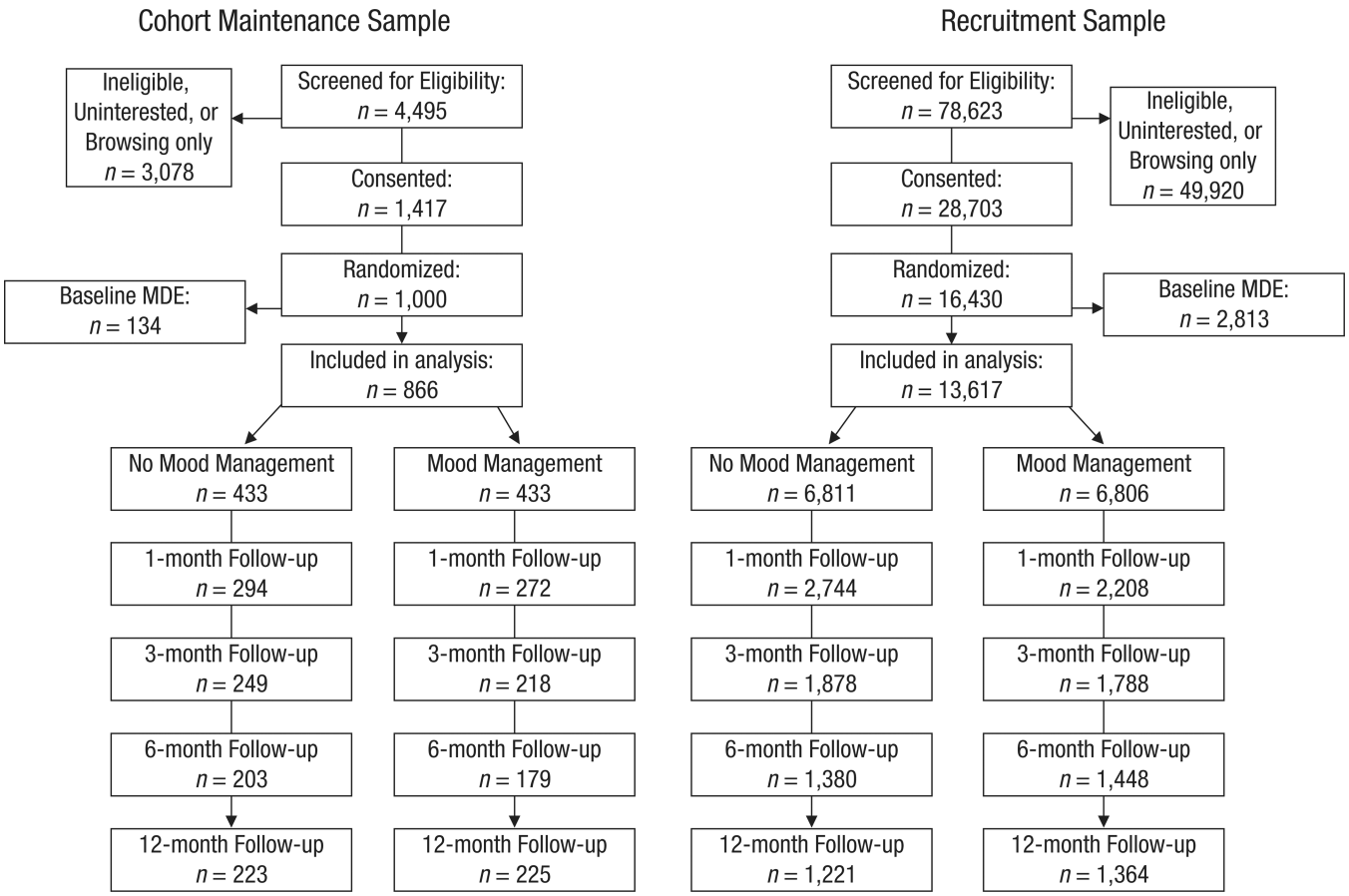

Fig. 1.

CONSORT diagram for progression of participants through the Internet trial.

Note: MDE = major depressive episode.

Table 1

Smoking Cessation Web Site Participants Not Meeting MDE Criteria, 2005–2009

	Cohort maintenance sample (*n* = 866)				Recruitment sample (*n* = 13,617)				
	No MM (*n* = 433)		MM (*n* = 433)		No MM (*n* = 6,811)		MM (*n* = 6,806)		
Variable	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***P*[a]**
Men	238	55.0	236	54.5	3,567	52.4	3,560	52.3	.17
Age									
18–34	197	45.5	214	49.5	3,387	49.8	3,286	48.4	.38
35–49	179	41.3	138	31.9	2,506	36.8	2,558	37.7	.73
50–64	54	12.5	71	16.4	855	12.6	907	13.4	.20
65 or older	3	0.7	9	2.1	55	0.8	43	0.6	.03
White	318	73.8	300	69.8	4,823	71.3	4,797	71.1	.67
Spanish language	207	47.8	209	48.3	5,342	78.4	5,348	78.6	< .001
Employed	323	74.6	334	77.3	5,439	79.9	5,496	80.8	.001
Married or partnered	238	55.0	248	57.2	3,766	55.4	3,789	55.8	.75
Some college or more	354	82.1	360	83.7	5,315	78.2	5,339	78.7	.002
CES-D > 16	156	36.0	146	33.7	2,403	35.3	2,350	34.5	.99
Past MDE	87	20.1	85	19.6	1,137	16.7	1,139	16.7	.02
High risk	195	45.0	181	41.8	2,932	43.1	2,877	42.4	.69
Number of MDEs at follow-ups									
0	363	83.8	367	84.8	6,197	91.0	6,154	90.4	< .001
1	48	11.1	47	10.9	477	7.0	477	7.0	< .001
>2	22	5.1	19	4.3	137	2.0	174	2.5	< .001

Note: MDE = major depressive episode; MM = mood management; CES-D = Center for Epidemiologic Studies Depression Scale.

[a] *p* values are Pearson chi-squares comparing cohort maintenance sample to recruitment sample.

Table 2

Rate of New MDE at Follow-Up

Sample	Mood management (%)	No mood management (%)
High risk (*n* = 6,185)	32.8	26.6
Cohort maintenance (*n* = 376)	32.1	28.5
Recruitment (*n* = 5,809)	32.9	26.4
Low risk (*n* = 8,276)	11.6	10.8
Cohort maintenance (*n* = 490)	8.6	11.1
Recruitment (*n* = 7,786)	12.0	10.8

Note: MDE = major depressive episode.