REVIEW

Two Decades of Smoking Cessation Treatment Research on Smokers with Depression: 1990–2010

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Received April 25, 2012; accepted August 22, 2012

ABSTRACT

Introduction: Adults with depression smoke at higher rates than other adults leaving a large segment of this population, who already incur increased health-related risks, vulnerable to the enormous harmful consequences of smoking. Yet, the impact that depression has on smoking cessation is not clear due to the mixed results of past research. The primary aims of this review were to synthesize the research examining the relationship of depression to smoking cessation outcomes over a 20-year period, to examine the gender and racial composition of these studies, and to identify directions for future research.

Methods: Potential articles published between January 1, 1990 and December 31, 2010 were identified through a MEDLINE search of the terms "clinical trial," "depression," and "smoking cessation." 68 studies used all three terms and met the inclusion criteria.

Results: The majority of studies examined either a past diagnosis of major depression or current depression symptoms. Within the few studies that examined the interaction of gender and depression on smoking cessation, depression had a greater impact on treatment outcomes for women than men. No study reported examining the interactive impact of race and depression on treatment outcomes.

Conclusions: Although attention to the relationship of depression and smoking cessation outcomes has increased over the past 20 years, little information exists to inform a treatment approach for smokers with Current Major Depressive Disorder, Dysthymia, and Minor Depression and few studies report gender and racial differences in the relationship of depression and smoking cessation outcomes, thus suggesting major areas for targeted research.

INTRODUCTION

The detrimental effects of cigarettes on the health of individuals and on costs to society are well-documented. Cigarette smoking is the single largest preventable cause of morbidity and mortality in Western countries. Tobacco use negatively impacts the health of every bodily system (USDHHS, 2004) and approximately 440,000 adults in the United States die each year from smoking-related illnesses. The annual economic cost of tobacco use to the United States is $196 billion (CDC, 2008).

Smoking and Depressive Disorders

Major Depressive Disorder (MDD) is one of the most common psychiatric illnesses in the United States with a lifetime prevalence of 16.2% and a 12-month prevalence of 5–9% (Kessler et al., 2003; Pratt & Brody, 2008; Ziedonis et al., 2008). Dysthymia and Minor Depression, like MDD, are also chronic mood disorders that affect a significant number of adults, cause substantial distress and impairment, and have important clinical implications. Dysthymia is defined by a depressed mood experienced for the majority of the time for at least 2 years along with additional symptoms of depression (e.g., sleep disturbance, low energy, low self-esteem; APA, 1994). Dysthymia is associated with significant impairment and a more severe course of later MDD (Keller, 1994; Klein & Santiago, 2003). Minor Depression, also referred to as subclinical, subthreshhold, or subsyndromal depression (Pincus, Davis, & McQueen, 1999), is included in the DSM-IV-TR (APA, 2002) as a Depressive Disorder Not Otherwise Specified and is defined by the report of symptoms of depression that are fewer in number than those needed for a diagnosis of MDD (APA, 2002). Minor Depression is associated with functional consequences (e.g., work and role impairment) that can equal those experienced with MDD (Ayuso-Mateos, Nuevo, Verdes, Naidoo, & Chatterji, 2010;

doi:10.1093/ntr/nts213
Advance Access publication October 25, 2012

Howland et al., 2008; Kessler, Zhao, Blazer, & Swartz, 1997; Lewinsohn, Solomon, Seeley, & Zeiss, 2000; Rowe & Rapaport, 2006; Wagner et al., 2000). The lifetime and 12-month prevalence of dysthymia are 6.8% and 1.6–2.5%, respectively (Ziedonis et al., 2008) and the lifetime prevalence of Minor Depression have been estimated to range from 10 to 24% (Judd, Rapaport, Paulus, & Brown, 1994; Kessler et al., 1997; Rowe & Rapaport, 2006).

Neurobiological, epidemiological, and clinical research all demonstrate significant relationships between smoking and depression (e.g., Mineur & Picciotto, 2010; Picciotto, Addy, Mineur, & Brunzell, 2008; Ziedonis et al., 2008). MDD and Dysthymia are associated with higher rates of smoking and nicotine dependence (Ajdacic-Gross et al., 2009; Dierker & Donny, 2008; Grant, Hasin, Chou, Stinson, & Dawson, 2004; Lasser et al., 2000; Morris, Giese, Turnbull, Dickinson, & Johnson-Nagel, 2006) while smokers are more likely to be diagnosed with depressive disorders; report greater symptoms and more frequent episodes of depression; and experience higher rates of suicide than nonsmokers (Katon et al., 2004; Wiesbeck, Kuhl, Yaldizli, Worst, & WHO/ISBRA Study Group on Biological State and Trait Markers of Alcohol Use and Dependence, 2008; Wilhelm, Wedgwood, Niven & Kay-Lambkin, 2006; Ziedonis et al., 2008). Further, adults with depressive disorders experience higher mortality, including mortality due to smoking-related illnesses (e.g., cardiovascular disease; Carney et al., 2008; Gallo et al., 2005; Lin et al., 2009; Whooley & Browner, 1998).

Quitting smoking can reduce the devastating and harmful consequences of smoking (Bunn, Stave, Downs, Alvir, & Dirani, 2006; CDC, 2002; USDHHS, 2001). Most smokers want to quit (CDC, 2011a), but are unable to succeed (Fiore et al., 2008; Shiffman, Brockwell, Pillitteri, & Gitchell, 2008). The role that depression plays in smoking cessation outcomes is not clear. Some studies suggest that smokers with a diagnosis or symptoms of depression have more difficulty quitting than other smokers (e.g., Anda et al., 1990; McClave et al., 2009; Niaura et al., 2001; Piper et al., 2010; Weinberger, Pilver, Desai, Mazure, McKee, 2012a, 2012b; Ziedonis et al., 2008). For example, our analyses of longitudinal, epidemiological data from the U.S. adult population found that current smokers with Current MDD, Lifetime MDD, Current Dysthymia, and Lifetime Minor Depression were less likely to report quitting smoking 3 years later (Weinberger et al., 2012a, 2012b). However, other studies find conflicting results (e.g., Hitsman, Borrelli, McChargue, Spring, & Niaura, 2003; Johnson & Breslau, 2006; Kassel, Yates, & Brown, 2007; Kinnunen et al., 2006).

Two meta-analyses have examined depression and smoking cessation outcomes. Hitsman et al. (2003) conducted a meta-analysis of 15 studies, published between 1988 and 2000, which evaluated the impact of a history of depression on smoking cessation outcomes in clinical trials. Short- and long-term abstinence rates did not differ by history of depression. The relationship between depression and smoking cessation outcome was not significant for either men or women in separate analyses by gender. An update of this analysis that included studies published through April of 2006 and limited the sample to participants receiving placebo found that while short-term abstinence rates did not differ by history of depression, smokers with a history of depression had poorer long-term cessation outcomes (Ziedonis et al., 2008). Results by race and gender were not reported. A second meta-analysis by Gierisch, Bastian, Calhoun, McDuffie, & Williams (2012) examined 16 studies of smoking cessation treatments for smokers with current or past depression published between 1994 and 2010. Gierisch et al. (2012) reported a small and positive effect of adding behavioral mood management to pharmacological treatments (relative risk = 1.41, 95% *CI* = 1.01, 1.96). The benefit of antidepressants on smoking cessation (antidepressants + behavioral treatments versus placebo + behavioral treatments) was not significant (relative risk = 1.31, 95% *CI* = 0.73, 2.34). The authors reported that they were not able to examine differences in outcomes by gender or type of depression (past vs. current) due to an insufficient number of studies for analysis. Results by race were not reported.

Smoking, Depression, and Gender

Approximately 20% of adult women in the United States between the ages of 18 and 65 years smoke (CDC, 2011b). Smoking resulted in more than 3 million premature deaths of women from 1980 to 2000 (USDHHS, 2001) and $30.6 billion of annual lost productivity from 1997 to 2001 (CDC, 2005). Women are more vulnerable than men to some of the health effects of smoking (e.g., lung cancer, heart disease) and lung cancer surpassed breast cancer as the leading cause of cancer-related deaths among women in 1987 (Ceribelli, Pino, & Cecere, 2007; Kiyohara & Ohno, 2010; Sarna & Bialous, 2004; USDHHS, 2001). Women also face gender-specific negative consequences of smoking including altered menstrual function, infertility, ectopic pregnancy, earlier menopause, and cancer of the cervix (USDHHS, 2001). Women appear to have more trouble quitting smoking than men (Perkins, 2001; Perkins & Scott, 2008; Wetter et al., 1999); however, few studies of smoking treatments examine outcomes by gender (Dickerson, Leeman, Mazure, & O'Malley, 2009; Piper, Fox, Welsch, Fiore, & Baker, 2001).

Women report higher rates of MDD and Dysthymia than men (Grant et al., 2004; Kessler, McGonagle, Swartz, Blazer, & Nelson, 1993; Kessler et al., 1994; Pratt & Brody, 2008). Moreover, women exhibit stronger relationships between depressive disorders (Current MDD, Lifetime MDD, and Minor Depression) and smoking (Husky, Mazure, Paliwal, & McKee, 2008; Paivarinta, Verkkoniemi, Niinisto, Kivela, & Sulkava, 1999); and are more likely to report smoking to manage negative affect (Fidler & West, 2009; Rundmo, Smedslund, & Gotestam, 1997; Wetter et al., 1999), to believe that smoking will reduce negative affect (Brandon & Baker, 1991), and to be concerned about managing negative affect after quitting (McKee, O'Malley, Salovey, Krishnan-Sarin, & Mazure, 2005). Together, this research suggests that gender differences would be important to examine in research on depression and smoking cessation treatments to understand how depression differentially impacts the quit behavior, and consequently the treatment needs, of men and women.

Smoking, Depression, and Race

Smoking-related diseases are the leading cause of mortality and morbidity among diverse ethnic groups, and minority groups report higher rates of some smoking-related illnesses (e.g., African-American men have higher rates of lung cancer as compared with Caucasian men; Fagan, Moolchan, Lawrence, Fernander, & Ponder, 2007; USDHHS, 1998). Differences in smoking rates (CDC, 2011b; USDHHS, 1998), duration of

smoking (Siahpush, Singh, Jones, & Timsina, 2010; Thompson, Moon-Howard, & Messeri, 2011), interest in quitting smoking (CDC, 2011a), and smoking quit rates (CDC, 2011a) have been reported by race (see USDHHS, 1998). Data from the CDC show that rates of current smoking are generally highest among Native American and Alaska Native adults (31.4%), followed by Caucasian (21.0%) and African-American (20.6%) adults, with Hispanic (12.5%) and Asian (9.2%) adults reporting the lowest levels of smoking (CDC, 2011b). Additional data from the CDC suggest that African-American smokers are more likely to report an interest in quitting smoking (75.6%) and making a quit attempt in the previous year (59.1%) than Caucasian (69.1% and 50.7%) and Hispanic (61.0% and 56.5%) smokers (CDC, 2011a). Minorities have been underrepresented in clinical smoking cessation research and few smoking cessation treatment studies report analyses by race (Dickerson et al., 2009; Piper et al., 2001). Further, the majority of the smoking cessation studies focused on racial minority groups have included African-American smokers with very few studies of Hispanic, Native American, Asian, or Pacific Islander smokers (Cox, Okuyemi, Choi, & Ahluwalia, 2011; Lawrence, Graber, Mills, Meissner, & Warnecke, 2003). Although pharmacological and behavioral interventions (e.g., nicotine replacement therapy, counseling) improve smoking cessation rates for African-American and Hispanic smokers (Webb, 2008; Webb, Rodrígeuz-Eequivel, & Baker, 2010), studies comparing quit rates between racial groups report mixed findings. Some studies find that Hispanic smokers are more likely to quit smoking (CDC, 2011a; USDHHS, 1998, see also Covey et al., 2008) and African-American smokers are less likely to quit smoking (Breslau, Johnson, Hiripi, & Kessler, 2001; CDC, 2011a; Covey et al., 2008; Cropsey et al., 2009; Piper et al., 2010; USDHHS, 1998) than Caucasian smokers. Other studies find no differences in cessation outcomes by race (Daza et al., 2006; Hyland et al., 2004; King, Polednak, Bendel, Vilsaint, & Nahata, 2004).

Comparisons of depression rates by race show mixed results. Studies have reported rates of depression for African Americans that are higher, lower, or not significantly different from Caucasians (Dunlop, Song, Lyons, Manheim, & Chang, 2003; Kessler et al., 1994; Pratt & Brody, 2008; Riolo, Nguyen, Greden, & King, 2005; Somervell, Leaf, Weissman, Blazer, & Bruce, 1989). Studies also find mixed results regarding the rates of depression among Hispanic subgroups as compared with Caucasians (Dunlop et al., 2003; Kessler et al., 1994; Riolo et al., 2005). In the few studies that have examined racial differences in the relationship between depression and smoking behavior, depressive symptoms were positively associated with smoking in Asian-American, Caucasian, and Hispanic adolescents (Gritz et al., 1998; Rosario-Sim & O'Connell, 2009; Way, Stauber, Nakkula, & London, 1994) but not in African-American adolescents (Gritz et al., 1998) or adolescents at a predominantly African-American and Puerto Rican/Dominican inner-city school (Way et al., 1994). Similar to gender, race is another important factor that may have important implications when examining the relationship of depression and smoking cessation outcomes.

Aims of the Current Review

Adults with depression smoke at higher rates than other adults leaving a large segment of this population, who already incur increased health-related risks, vulnerable to the enormous personal and societal consequences of smoking. The impact that depression has on smoking cessation outcomes is not clear from past research. Past meta-analytic reviews on this topic have been necessarily limited by the inclusion criteria for formal statistical analyses. A broad and comprehensive review of published studies on depression and smoking cessation outcomes, critical to understand the current state of the field, has not yet been conducted. In addition, little is known about the smoking behavior of smokers with depressive disorders other than past depression (e.g., smokers with current depression or minor depression). Further, mixed results have been reported regarding gender and racial differences in smoking behavior and meta-analytic reviews of depression and smoking cessation outcomes have been limited in their ability to closely examine gender or race. Understanding how depression has been studied in past smoking cessation research is critical to direct lines of future research. The primary aims of this review are: (a) to synthesize the research on smoking cessation outcomes by depression over a 20-year period, (b) to examine the gender and racial composition of studies examining the role of depression in smoking cessation outcomes, and (c) to use this review to identify directions for future research.

METHODS

We conducted a MEDLINE search using the terms "clinical trial," "depression," and "smoking cessation" to identify papers published between January 1, 1990 and December 31, 2010. After removing duplicate articles, the remaining articles were individually examined to determine whether they met inclusion criteria, namely, that they (a) were clinical trials for smoking cessation, (b) assessed depression at baseline, (c) analyzed endpoint smoking outcomes by depression, and (d) were published in English.

Information was then gathered from each paper that met the criteria to be included in the review: location of research (country), type of funding, sample (e.g., general population versus a subgroup of smokers), sample size, gender composition, racial composition, mean age, type of smoking treatment(s), type of depression assessed (e.g., depressive symptoms, diagnosis of MDD), exclusion criteria related to depression (e.g., current depression, current use of antidepressant medications), and whether gender or race was covaried for or included as an interaction term in the analyses of depression and smoking outcomes.

In addition to frequency and descriptive statistics, differences by type of study and whether studies found a significant impact of depression on smoking cessation outcomes were examined using *t*-tests for continuous variables and chi-squares for categorical variables. Statistical analyses were conducted using SPSS v.16.0 software for PC (SPSS, Inc.). Statistical tests were two-tailed and differences were considered significant when $p < .05$.

RESULTS

Study Characteristics

General Study Characteristics

A total of 190 articles published between 1990 and 2010 were identified through the literature search and individually

examined. Of the 190 articles, 68 (36%) met all the criteria to be included in the review. Table 1 shows a summary of characteristics for studies that examined smoking cessation outcomes for adults with depression as compared with adults without depression (DEP/CON, $n = 57$) and Table 2 shows a summary of characteristics for studies that examined smoking cessation outcomes within samples were restricted to only adults with depression (DEP/DEP, $n = 11$). An increasing number of articles examined smoking cessation treatment and depression over time (1990–1994, $n = 3$; 1995–1999, $n = 13$; 2000–2004, $n = 19$; 2005–2010, $n = 33$). Sixty-five percent of studies included a general sample of smokers while 35% of studies examined a subgroup of smokers (e.g., smokers with medical illnesses, adolescent smokers; see Tables 1 and 2).

Funding Agency

Nearly two-third of studies (64.7%; $n = 44$) reported a single source of funding while 25% reported multiple sources and 10.3% did not report a funding source. Government agencies were the most common source of funding ($n = 52$, 85.2% of studies that listed at least one source of funding) Additional sources of funding were pharmaceutical companies ($n = 12$), private foundations ($n = 9$), and university sources ($n = 5$). The majority of the research was conducted in the United States (88.2%) with additional research conducted in the Netherlands, Germany, France, Turkey, and Iceland. Two studies, led by researchers located in the United States, collected data in multiple countries.

Sample Size (Tables 1 and 2)

The sample sizes of the reviewed studies ranged from 25 to 3,056 with a mean sample size of 402 ($SD = 497$) and a median sample size of 250.

Mean Age of Participants

Forty-nine studies reported the average age of their participant sample (range = 16–59 years old) and three-quarter of the mean ages fell between 40 and 49 years.

Gender Composition (Tables 1 and 2)

Sixty-nine out of 70 studies reported the gender composition of their sample. On average, 55% of the participants were female (range = 19–100%).

Racial Composition (Tables 1 and 2)

Forty-eight studies reported the racial composition of their samples, collected data in the United States (i.e., allowed for consistent labeling of racial categories), and did not specifically limit their sample to one racial group (e.g., African-American smokers). On average, 80% of the participants in these samples were identified as Caucasian (median = 87%). Five studies reported that Caucasians made up less than 50% of their samples (Cinciripini et al., 2010, 33.5%; Killen et al., 2004, 46.5%; MacPherson et al., 2010, a maximum of 27.3%; Sonne et al., 2010, 38.2%; Vidrine, Arduino, & Gritz, 2006, 18.9%). Two samples consisted of adult African-American smokers (Catley, Ahluwalia, Resnicow, & Nazir, 2003; Catley, Harris, Okuyemi, Mayo, Pankey, & Ahluwalia, 2005) and one sample consisted of adult Spanish-speaking Latino smokers (Muñoz, Marin, Posner, & Pérez-Stable, 1997).

Assessment of Depression

Fifty-seven articles (83.8%) compared smoking cessation treatment outcomes for adults with depression and a control group (DEP/CON) either by diagnosis (e.g., participants with a lifetime diagnosis of MDD as compared with participants without a lifetime diagnosis of MDD; $n = 32$) or symptoms (e.g., participants with higher current depressive symptoms as compared with participants with lower current depressive symptoms; n = 35; Table 1). Ten studies that reported outcomes by both diagnosis and symptoms were included in totals above. All articles that examined outcomes by diagnosis except for two focused on Lifetime MDD (two of these studies also reported outcomes by Current MDD). Half of the DEP/CON studies explicitly reported that Current MDD ($n = 29$) was an exclusion criteria while one-third excluded potential participants for current antidepressant use ($n = 21$).

The 11 remaining articles examined the outcomes of two or more smoking cessation treatments in samples that included only adults with depression (DEP/DEP; Table 2). Similar to the DEP/CON articles, the majority of these studies focused on a lifetime history of MDD (64%) while the remaining studies examined current depression (Current MDD or current depression symptoms, 36%). Over half of these studies ($n = 6$) stated that Current MDD was an exclusion criteria while 82% ($n = 9$) excluded potential participants who were currently taking antidepressants.

Depression and Smoking Cessation Treatment Outcomes

Tables 1 and 2 show the treatment category (pharmacological, behavioral, combined, others) and specific treatment that was the primary comparison in outcome analyses. All of the U.S. FDA-approved pharmacotherapy treatments for nicotine dependence, except for nicotine lozenge, were included in at least one study. Transdermal nicotine patch and bupropion were the most commonly administered pharmacological treatments. Behavioral treatments were most commonly labeled as behavioral, cognitive–behavioral, mood management, or motivation-based therapy. Therapies were administrated in a range of formats including in-person individual and group counseling, on-line/internet, by phone, and by mail.

Twenty-two out of 57 DEP/CON papers reported that at least some of the primary treatment outcomes differed by depression status (a diagnosis of depression/greater depressive symptoms versus no diagnosis of depression/fewer depressive symptoms) with the majority finding worse outcomes for smokers with a diagnosis or greater symptoms of depression (Table 1). Studies that found depression-related differences in smoking cessation outcomes did not differ from studies that did not find differences by the year of publication ($\chi^2 = 16.2$, $df = 17$, $p = .51$), type of funding source ($\chi^2 = 1.58$, $df = 3$, $p = .66$), sample size ($t = .03$, $df = 57$, $p = .98$), whether their main comparison was a pharmacological or behavioral treatment ($\chi^2 = 1.18$, $df = 1$, $p = .43$), or by whether the studies assessed depression by symptoms or diagnosis ($\chi^2 = 1.72$, $df = 2$, $p = .42$). Studies that found differences in outcomes by depression and those that did not find significant differences reported similar gender (54% vs. 52% female participants) and racial (72% vs. 71% Caucasian participants) compositions ($p > .05$).

Table 1. Study Characteristics for Studies That Compared Smoking Treatment Outcomes for Smokers With and Without Depression

First author	Year	Sample size	Sub-group[a]	% Female	% Caucasian	Type of depression[b]	Type of diagnosis	Treatment category[c]	Specific treatment[c]	Outcome (by depression)[d]	Outcome (by treatment)[e]
Covey	1993	220	—	53	—	Diagnosis	Lifetime MDD	Behavioral	Behavioral Therapy	3	—
Glassman	1993	300	—	56	87	Diagnosis	Lifetime MDD	Pharmacological	Clonidine	1	4
Hall	1994	149	—	52	88	Diagnosis	Lifetime MDD	Behavioral	Cognitive–Behavioral Mood Management Treatment	3	1
Ginsberg	1995	62	—	55	90	Diagnosis	Lifetime MDD	Behavioral	Aversive Smoking and Relapse Prevention Skills Training	1	4
Kinnunen	1996	269	—	51	82	Symptoms	—	Pharmacological	Nicotine Gum	1	1
Muñoz	1997	136	6	38	0	Diagnosis, Symptoms	Lifetime MDD, Current MDD	Behavioral	Mood Management Intervention Program	4	4
Colby	1998	40	1	58	65	Symptoms	—	Behavioral	Motivational Interviewing	2	—
Hall	1998	199	—	55	87	Diagnosis	Lifetime MDD	Combined	Nortriptyline, Cognitive–Behavioral Therapy	1	3
Prochazka	1998	214	—	38	82	Diagnosis, Symptoms	Lifetime MDD	Pharmacological	Nortriptyline	3	—
Blondal	1999	100	—	62	—	Symptoms	—	Pharmacological	Fluoxetine	1	1
Covey	1999	68	—	63	—	Diagnosis	Lifetime MDD	Pharmacological	Naltrexone	2	1
Hayford	1999	615	—	55	—	Diagnosis, Symptoms	Lifetime MDD	Pharmacological	Bupropion	3	—
Hitsman	1999	253	—	59	97	Diagnosis	Lifetime MDD	Pharmacological	Fluoxetine	4	1
Killen	1999	408	—	41	83	Symptoms	—	Pharmacological	Transdermal Nicotine Patch	1	—
Keuthen	2000	120	—	62	—	Diagnosis, Symptoms	Lifetime MDD	Pharmacological	Fluoxetine	3	—
Killen	2000	224	—	46	88	Diagnosis	Lifetime MDD	Pharmacological	Paroxetine	3	—
Niaura	2001	267	—	55	——	Diagnosis, Symptoms	Lifetime MDD	Pharmacological, Behavioral	Study 1: Clonidine, Study 2: Fluoxetine, Study 3: self-help material	1	—
Patten	2002	51	3	47	94	Symptoms	—	Behavioral	Cognitive–Behavioral Mood Management Treatment	—	2

(Continued)

Table 1. Continued

First author	Year	Sample size	Sub-group[a]	% Female	% Caucasian	Type of depression[b]	Type of diagnosis	Treatment category[c]	Specific treatment[c]	Outcome (by depression)[d]	Outcome (by treatment)[e]
Catley	2003	498	5	60	0	Symptoms	—	Behavioral	Culturally Sensitive Quitting Materials	3	—-
Cinciripini	2003	121	—	71	91	Symptoms	—	Pharmacological	Transdermal Nicotine Patch	1	—
Killen	2003	224	—	46	—	Diagnosis	Lifetime MDD	Pharmacological	Peroxetine	3	—
Mermelstein	2003	756	—	66	42	Diagnosis	Lifetime MDD	Behavioral	Tailored Telephone Counseling	1	3
Smith	2003	893	—	52	—	Diagnosis	Lifetime MDD	Pharmacological	Transdermal Nicotine Patch, Bupropion	3	1
Swan	2003	1524	—	57	90	Diagnosis, Symptoms	Lifetime MDD	Combined	Bupropion, Behavioral Counseling	1	—
Cox	2004	783	—	54	97	Diagnosis	Lifetime MDD	Pharmacological	Bupropion	3	3
Haas	2004	549	—	54	90	Diagnosis	Lifetime MDD	Behavioral	Cognitive–Behavioral Therapy	3	4
Horn	2004	258	1	56	93	Symptoms	—	Behavioral	Group Skills Training Counseling	3	1
Killen	2004	211	1	31	47	Diagnosis	Lifetime MDD	Pharmacological	Bupropion	3	—
Lerman	2004	299	—	54	64	Symptoms	—	Pharmacological	Transdermal Nicotine Patch, Nicotine Nasal Spray	3	3
Saules	2004	150	—	55	73	Diagnosis, Symptoms	Lifetime MDD	Pharmacological	Fluoxetine	3	3
Catley	2005	600	5	60	0	Symptoms	—	Pharmacological	Bupropion	3	3
Wagena	2005	255	2	51	—	Symptoms	—	Pharmacological	Bupropion, Nortriptyline	4	4
Berlin	2006	600	—	48	85	Symptoms	—	Pharmacological	Befloxatone	1	—
Blalock	2006	81	4	100	80	Diagnosis	Current Dysthymia, Current Minor Depression	Behavioral	Video Skills Training Counseling	1	—
Vidrine	2006	95	2	22	19	Symptoms	—	Behavioral	Cell Phone Counseling Intervention	1	—
Brown	2007	524	—	48	92	Diagnosis, Symptoms	Lifetime MDD	Combined	Cognitive–Behavioral Mood Management Treatment, Bupropion	3	3

(Continued)

Table 1. Continued

First author	Year	Sample size	Sub-group[a]	% Female	% Caucasian	Type of depression[b]	Type of diagnosis	Treatment category[c]	Specific treatment[c]	Outcome (by depression)[d]	Outcome (by treatment)[e]
Japuntich	2007	677	—	57	95	Diagnosis	Lifetime MDD, Current MDD	Behavioral	Cognitive Behavior/ Skills Training, Motivational Interviewing	1	—
Oncken	2007	152	4	100	89	Diagnosis	Lifetime MDD	Pharmacological	Transdermal Nicotine Patch	1	—
Stein	2007	383	3	47	78	Symptoms	—	Behavioral	Motivational Interviewing + Skills Training	3	—
Uyar	2007	131	—	19	—	Symptoms	—	Pharmacological	Transdermal Nicotine Patch, Bupropion	1	—
Carmody	2008	286	—	39	69	Diagnosis	Lifetime MDD	Other	Hypnosis	2	1
Kinnunen	2008	608	—	51	81	Symptoms	—	Pharmacological	Nicotine gum	3	1
Kodl	2008	462	3	32	77	Symptoms	—	Combined	Nicotine Replacement Therapy, Behavioral Therapy	3	—
Thorndike	2008	245	2	29	95	Symptoms	—	Pharmacological	Bupropion	1	1
Trockel	2008	1233	2	38	67	Diagnosis	Current MDD, Dysthymia, or Minor Depression	Behavioral	Cognitive–Behavioral Therapy	3	2
Walsh	2008	110	—	49	65	Symptoms	—	Pharmacological	Naltrexone	1	1
McClure	2009	1177	—	71	95	Diagnosis	Lifetime MDD	Behavioral	Behavioral Therapy	3	—
Muñoz	2009	1000	—	45	70	Diagnosis	Lifetime MDD, Current MDD	Behavioral	Emails, Mood Management Intervention Program, "Bulletin Board" groups	3	—
Batra	2010	268	—	—	—	Symptoms	—	Combined	Counseling and medication (e.g., transdermal nicotine patch, nicotine gum, bupropion) matched to patient	3	1

(Continued)

Table 1. Continued

First author	Year	Sample size	Sub-group[a]	% Female	% Caucasian	Type of depression[b]	Type of diagnosis	Treatment category[c]	Specific treatment[c]	Outcome (by depression)[d]	Outcome (by treatment)[e]
Cinciripini	2010	266	4	100	34	Symptoms	—	Behavioral	Cognitive Behavioral Analysis System of Psychotherapy	2	1
Hayes	2010	237	2	54	81	Symptoms	—	Behavioral	Motivational Enhancement	3	—
Kapson	2010	100	—	51	65	Depression Proneness	—	Behavioral	Cognitive–Behavioral Therapy	2	1
McClure	2010	542	—	65	89	Diagnosis	Lifetime MDD	Behavioral	Cognitive–Behavioral Therapy	3	—
Schnoll	2010	246	2	48	66	Symptoms	—	Pharmacological	Bupropion	1	1
Seidman	2010	2153	—	69	88	Symptoms	—	Behavioral	Internet Counseling	3	3
Sonne	2010	225	3	48	38	Diagnosis, Symptoms	Lifetime MDD	Combined	Transdermal Nicotine Patch, Cognitive–Behavioral Counseling	1	—
Torres	2010	3056	—	53	74	Diagnosis, Symptoms	Lifetime MDD	Behavioral	Emails, Mood Management Intervention Program, "Bulletin Board" groups	1	—

—: not applicable, not reported, or unable to calculate from data available.

[a]Subgroup: 1 = Adolescents, 2 = Adults with a Medical Illness (e.g., cancer, heart disease, HIV), 3 = Adults with an Alcohol or Substance Use Disorder, 4 = Women (e.g., women, pregnant woman, menopausal women), 5 = African-American Adults, 6=Spanish-speaking Hispanic Adults.

[b]Primary type(s) of depression examined in the analyses of smoking cessation outcomes.

[c]Primary category and type of treatment compared in the analyses of outcomes. Other types of treatments may have been offered (e.g., pharmacological studies may have offered counseling to all participants; behavioral studies may have offered nicotine replacement therapy to all participants).

[d]Outcome (by Depression): Differences in primary smoking abstinence outcome(s after treatment by depression (comparison primary treatment outcomes for smokers with and without depression): 1 = smokers with depression/higher depression symptoms had worse smoking outcomes than smokers without depression/lower depression symptoms, 2 = smokers with depression/higher depression symptoms had better smoking outcomes than smokers without depression/lower depression symptoms, 3 = smokers with and without depression had equivalent smoking outcomes, 4 = mixed outcomes on primary outcomes. Where multiple outcomes were listed, the study was rated as showing a difference if there was a difference by depression on at least one major outcome for the overall sample and/or for the group receiving the Specific Treatment listed in the table.

[e]Outcome (by Treatment): Differences in primary smoking abstinence outcome(s) for smokers with depression in treatment versus control conditions: 1 = better smoking abstinence outcomes in treatment condition versus control, 2 = worse smoking abstinence outcomes in treatment condition versus control, 3 = no difference in smoking abstinence outcomes in treatment condition versus control, 4 = mixed outcomes on primary outcomes. Where multiple outcomes were listed, the study was rated as showing a difference if there was a difference on at least one major outcome.

Table 2. Study Characteristics for Studies That Examined Smoking Treatment Outcomes for Samples With Depression

First author	Year	Sample size	Sub-group[a]	% Female	% Caucasian	Type of depression[b]	Treatment category[c]	Specific treatment[c]	Outcome by treatment[d]
Hall	1996	201	—	52	92	Lifetime MDD Diagnosis	Behavioral	Mood Management Intervention	3
Patten	1998	29	3	52	97	Lifetime MDD Diagnosis	Behavioral	Cognitive–Behavioral Mood Management	4
Brown	2001	179	—	60	97	Lifetime MDD Diagnosis	Behavioral	Cognitive–Behavioral Therapy for depression	3
Chengappa	2001	25	2	72	92	Lifetime MDD Diagnosis	Pharmacological	Bupropion	—
Thorsteinsson	2001	38	—	47	84	Current MDD Diagnosis	Pharmacological	Transdermal Nicotine Patch	1
Covey	2002	134	—	63	88	Lifetime MDD Diagnosis	Pharmacological	Sertraline	3
Hall	2006	322	—	70	68	Current MDD Diagnosis	Combination	Staged Care Intervention	1
Evins	2008	199	—	49	—	Current or Lifetime MDD Diagnosis	Pharmacological	Bupropion	3
Vickers	2009	60	1	100	98	Current MDD	Behavioral	Exercise Intervention	3
Macpherson	2010	68	—	48	—	Current Depression Symptoms	Behavioral	Behavioral Activation Treatment for Smoking	1
Van Der Meer	2010	485	—	62	—	Lifetime MDD Diagnosis	Behavioral	Mood Management Counseling	1

—: not applicable, not reported, or unable to calculate from data available.

[a]Subgroup of adults with depression: 1 = Women with depression (e.g., women, pregnant woman, menopausal women), 2 = Adults with depression receiving SSRI treatment, 3 = Adults with depression and a comorbid Alcohol or Substance Use Disorder.

[b]Type(s) of depression that was the inclusion criteria for this study.

[c]Primary category and type of treatment compared to a control treatment condition in the analyses of outcomes. Other types of treatments may have been offered (e.g., pharmacological studies may have offered counseling to all participants; behavioral studies may have offered nicotine replacement therapy to all participants).

[d]Differences in primary smoking abstinence outcome(s): 1 = better smoking abstinence outcomes in treatment condition versus control, 2 = worse smoking abstinence outcomes in treatment condition versus control, 3 = no difference in smoking abstinence outcomes in treatment condition versus control, 4 = mixed outcomes on primary outcomes. Where multiple outcomes were listed, the study was rated as showing a difference if there was a difference on at least one major outcome.

Of the articles that compared smokers with depression on treatment outcomes of a specific treatment versus a control/comparison treatment, 50% of DEP/CON articles and 40% of DEP/DEP articles reported that smokers with depression achieved better abstinence rates with the treatment of interest as compared with the control treatment while 26% of DEP/CON articles and 50% of DEP/DEP articles found no differences in abstinence outcomes for the treatment of interest versus the control treatment (Tables 1 and 2).

Gender and the Analyses of Depression and Smoking Cessation Outcomes

Thirteen studies controlled for gender in their analysis of depression and smoking cessation outcomes (Berlin & Covey, 2006; Brown et al., 2001; Cinciripini et al., 2003; Japuntich et al., 2007; Kodl et al., 2008; MacPherson et al., 2010; McClure et al., 2009; McClure et al., 2010; Niaura et al., 2001; Schnoll et al., 2010; Thorndike et al., 2008; Trockel, Burg, Jaffe, Barbour, & Taylor, 2008; Walsh, Epstein, Munisamy, & King, 2008) while seven studies examined gender differences in the relationship between depression and smoking cessation outcomes (Covey, Glassman, & Stetner, 1999; Covey, Glassman, Stetner, & Becker, 1993; Glassman et al., 1993; Hall et al., 1998; Japuntich et al., 2007; Kinnunen, Korhonen, & Garvey, 2008; Swan et al., 2003). Five studies found gender differences in the relationship of depression and treatment outcomes (Covey et al., 1999; Covey et al., 1993; Glassman et al., 1993; Hall et al., 1998; Swan et al., 2003) while two studies did not find significant gender differences (Japuntich et al., 2007; Kinnunen et al., 2008).

Among studies that found significant gender differences, depression had a greater impact on treatment outcomes for women than men. A study of bupropion and behavioral treatment (Swan et al., 2003) found that while a history of depression was significantly associated with smoking 1 year after treatment for both men and women in the univariate analyses, the association remained significant for men only in the stepwise analyses. A placebo-controlled study of naltrexone (Covey et al., 1999) found that the effect of naltrexone was greater for women with a history of depression than men with a history of depression. It should be noted that women with a history of depression had a lower smoking cessation rate than men with depression (44% vs. 80%) but had a greater treatment effect due to a much lower placebo response rate in women than men (0% vs. versus 60%). There was no gender difference in the efficacy of naltrexone for men and women without a history of depression. The gender by depression interaction was also examined in a study of nortriptyline (versus placebo) and cognitive-behavioral therapy (vs. health education; Hall et al., 1998). Women with a history of depression had poorer outcomes than women without a history of depression. History of depression did not significantly predict outcome for men. A placebo-controlled study of clonidine (Glassman et al., 1993) found a significant effect of clonidine on smoking cessation at the end of treatment only in female participants with a history of depression while an analysis of participants receiving placebo in a clinical trial of clonidine (Covey et al., 1993) found differences in cessation outcomes by depression status for men (history of depression, 20%; no history of depression, 32%) but not for women (history of depression, 23%; no history of depression, 25%).

Race and the Analyses of Depression and Smoking Cessation Outcomes

Six studies controlled for race in their analysis of depression and smoking cessation outcomes (Berlin & Covey, 2006; Cinciripini et al., 2003; Kodl et al., 2008; McClure et al., 2009; Thorndike et al., 2008; Trockel et al., 2008). No study reported analyzing racial differences in the relationship between depression and smoking cessation outcomes. As noted above, the majority of samples were composed primarily of Caucasian participants thus limiting the ability of researchers to examine outcomes by race.

Two studies examined smoking cessation in adult African-American smokers (Catley et al., 2003, 2005). One study (Catley et al., 2003) did not find a significant relationship between baseline depression symptoms and cessation outcomes in a sample of 498 smokers who received nicotine replacement therapy with either culturally-sensitive or standard self-help smoking cessation materials. The second study (Catley et al., 2005) also found no relationship between baseline depression symptoms and smoking cessation outcomes for a sample of 600 smokers who received bupropion or placebo. In both studies, depression symptoms at the time of the follow-up analyses were associated with decreased likelihood of being abstinent from smoking at that time (e.g., depression symptoms at Month 6 and smoking status at Month 6). One study of 136 adult Spanish-speaking Latino smokers (Muñoz et al., 1997) reported that smokers with a history of depression, but not currently depressed, who concurrently received a smoking cessation guide plus a mood management intervention reported higher rates of smoking abstinence than those who received the smoking cessation guide first and the mood management intervention 3 months later.

DISCUSSION

High rates of smoking in the third of the U.S. population that will be affected by a depressive disorder over a lifetime makes it critically important to understand how depression impacts smoking cessation outcomes, and how and what interventions improve smoking cessation outcomes for adults with depression. This article is the first to broadly review 20 years of available research on the relationship of depression and smoking cessation outcomes. This review, which allowed for the inclusion of more than four times as many articles as past meta-analytic reviews of the same time period, presents the most comprehensive examination to date of the state of research on depression and smoking cessation outcomes. Further, this review was able to gather and synthesize information about gender and race that has not been possible to examine within formal meta-analytic reviews due to the highly limited data available in the extant literature. Although an increasing number of investigations over time have examined the relationship of depression on smoking outcomes for a variety of pharmacological and behavioral treatments, there are critical gaps in the literature that future research can address.

First, the majority of research studies on depression and smoking cessation outcomes focused on Lifetime MDD (Gierisch et al., 2012; Ziedonis et al., 2008). Very little is known about how Current MDD, Dysthymia, and Minor Depression affect smoking cessation. Yet, there is a positive relationship

between diagnoses of Current MDD, Dysthymia, and Minor Depression and smoking behavior (Katon et al., 2004; Lasser et al., 2000). These findings are accompanied by epidemiological evidence that Current MDD, Current Dysthymia, and Minor Depression are associated with difficulty quitting smoking (Lasser et al., 2000; Weinberger et al., 2012a, 2012b) and by neurobiological data showing that depressive symptoms and smoking share a common neural pathway in the brain through nicotinic acetylcholine receptors (nAChRs, Mineur et al., 2010; Picciotto, Brunzell, & Caldarone, 2002).

Beyond smoking and depression sharing neural pathways, antidepressants have affinity for nAChRs, and nicotinic agents have been proposed as potential therapeutic targets for depression (e.g., Mineur et al., 2010; Picciotto et al., 2002; Shytle et al., 2002). Many studies in our review excluded smokers taking antidepressants. We previously found that few studies examine antidepressant drug response by smoking status (Weinberger, McKee, Picciotto, & Mazure, 2011) and, conversely, few studies examine the impact of antidepressants on smoking cessation outcomes although preliminary data suggest that smokers taking antidepressants have more trouble quitting (Gravely-Witte, Stewart, Suskin, & Grace, 2009; Japuntich et al., 2007; Weinberger, McKee, & George, 2012). It remains unclear how smokers taking antidepressants respond to pharmacological and behavioral smoking cessation treatments that have been found to be effective in general populations (Fiore et al., 2008).

Second, few studies have examined the interactive impact of gender and depression on smoking cessation outcomes consistent with reviews showing that smoking treatment research rarely examine outcomes by gender (Dickerson et al., 2009; Piper et al., 2001). Women appear to have more trouble quitting smoking than men (Perkins, 2001; Perkins & Scott, 2008; Schnoll, Patterson, & Lerman, 2007; Wetter et al., 1999) and the majority of studies in this review that considered gender reported that depression had a greater negative impact on smoking cessation outcomes for women as compared with men. Gender differences were found for several pharmacological agents (e.g., naltrexone, clonidine, and nortriptyline; Covey et al., 1999; Glassman et al., 1993; Hall et al., 1998) and additional research examining gender difference is needed for both pharmacological and behavioral treatments. Our analyses of epidemiological data (Weinberger et al., 2012a, 2012b) found that overall smoking cessation rates over a 3-year period in the general U.S. adult population were similarly impacted by depression for men and women, however, depression would still be expected to have a greater impact on female smokers due to the fact that women experience depression at higher rates than men (Grant et al., 2004). At this time, treatments and treatment-related variables that can be used to best help women with depression to successfully quit smoking are still not identified.

Third, no study included in this review examined racial differences in the relationship between depression and smoking cessation. Most studies included a small number of participants from minority groups, or included samples that were entirely from a minority population, both of which preclude the statistical analysis of outcomes by race. One study published in 2011 (Castro et al., 2011) found that higher baseline depressive symptoms were associated with lower quit rates at 1, 2, and 4 weeks for Caucasian and African-American smokers, but not Hispanic smokers, in a sample of 389 adults (n = 133 Caucasian, n = 130 African Americans, n = 126 Hispanic) receiving counseling, self-help materials, and transdermal nicotine patch. This study shows that racial differences can exist in the relationship of depression and smoking cessation outcomes and highlights the importance of having more studies that are able to analyze outcomes of smoking treatments by race.

Minorities have been underrepresented in research on substance abuse treatments (Burlew et al., 2011) including smoking treatments (Dickerson et al., 2009; Fiore et al., 2008; Piper et al., 2001). Smokers from minority groups are motivated to stop smoking and willing to participate in research studies (Cox et al., 2011). However, a recent report found that while African-American smokers were more likely than Caucasian smokers to contact staff for a smoking cessation clinical trial, they were almost three times less likely to be enrolled than Caucasians due both to ineligibility based on entrance criteria and not attending screening and study appointments (King, Cao, Southard, & Matthews, 2011). Increasing the recruitment of minorities into smoking cessation trials requires significant resources and targeted efforts including community involvement and culturally sensitive and tailored approaches to recruitment (e.g., language, diverse research staff; Burlew et al., 2011; King et al., 2011). Examining race in smoking outcomes also requires attention to the interaction of additional factors such as socioeconomic status and gender (Burlew et al., 2011; King et al., 2011; Thompson et al., 2011; USDHHS, 1998).

Although it is important to compare the impact of depression on smoking cessation by race, it is also important to determine how variables that may be unique to different racial groups (e.g., racial/ethnic identity, acculturation, culture-specific values, stressors, coping styles; Piper et al., 2001; USDHHS, 1998) impact smoking cessation outcomes to determine the best ways to improve smoking cessation outcomes. One study of African-American smokers included in the review utilized culturally sensitive smoking cessation materials (Catley et al., 2003); however, primary analyses suggested no differences in smoking outcomes for culturally sensitive materials as compared with standard materials (reported in Ahluwalia, Richter, Mayo, & Resnicow, 1999). Researchers are currently working to develop culturally sensitive smoking interventions for diverse minority groups (e.g., D'Silva, Schillo, Sandman, Leonard, & Boyle, 2011; Webb, 2009; Wu, Ma, Zhou, Zhou, Liu, & Poon, 2009; Zinser, Pampel, & Flores, 2011) suggesting that a focus on this important area of research will continue to grow in the future.

Fourth, studies that have attempted to improve smoking cessation outcomes for smokers with depression have focused on the impact of depression-related aspects of treatment, such as the use of antidepressant medications or mood-focused cognitive-behavioral therapies. A recent meta-analysis (Gierisch et al., 2012) found that the effect of adding mood management counseling to other behavioral smoking cessation treatment on smoking outcomes was small but positive, while the effect of providing antidepressants was not significant. It may be useful for future research to focus on behavioral interventions that exploit smoking-related differences between smokers with and without depression. For example, smokers with depression report greater tobacco withdrawal (Breslau, Kilbey, & Andreski, 1992; Weinberger, Desai, & McKee, 2010), cue reactivity (Pomerleau et al., 2005; Weinberger, McKee, & George, 2012), smoking reward (Spring, Pingitore, & McChargue, 2003), and endorsement of smoking expectancies, including negative

affect reduction (Currie, Hodgins, el-Guebaly, & Campbell, 2001; Weinberger, George, & McKee, 2011). Further, neurobiological findings related to the common pathways of nicotine and depression through the nAChR system suggest that smokers with depression would experience greater cravings to smoke when attempting to quit (Benowitz, 2008; Mineur et al., 2010; Picciotto et al., 2002). Thus, smokers with depression may benefit from behavioral or pharmacological (or combined) interventions with an enhanced focus on cravings and withdrawal in order to improve success with quitting smoking.

Although this review attempted to be as inclusive as possible with regard to studies that examined depression and smoking cessation outcomes, it was limited to studies that were published, studies that were available through a MEDLINE search, and data that were reported within each reviewed study. Studies that found negative relationships between depression and smoking cessation outcomes may not have been published and analyses of the interaction of depression and gender or race may have been conducted but not reported. The Clinical Equity Provision of the 1993 National Institutes of Health Revitalization Act (Public Law 103-43; Federal Register, 1994) requires that women and minorities be considered for inclusion in all National Institutes of Health-funded human subject research with the goal of increasing knowledge about gender and racial differences in research on human subjects. As discussed above, gender and racial differences in smoking cessation outcomes are rarely published (e.g., Piper et al., 2001) and the ability to examine racial differences is limited by the inclusion of minority populations in samples. Because there are gender and racial differences in smoking and depression, analyzing and publishing outcomes by gender and race, when possible, would provide important information for both researchers and clinical treatment providers.

CONCLUSIONS

Attention to the relationship of depression to smoking cessation outcomes has increased over the past 20 years. Yet, there is a very limited knowledge base on the relationship of current MDD, Dysthymia, Minor Depression, and antidepressants to smoking cessation treatments and outcomes. There also is little available data on gender and racial differences in the relationship of depression to smoking cessation outcomes. Research in these areas is required in order to target treatments and guide treatment development with important subgroups of smokers with depression.

FUNDING

This work was supported by the National Institutes on Health (R03-DA027052 to A.H.W., P50-DA033945 [ORWH & NIDA] to S.A.M., NIH/NIGMS SDSU MARC T34-GM008303 to A.M.); Women's Health Research at Yale; the Yale Cancer Center; and the State of Connecticut, Department of Mental Health and Addiction Services.

DECLARATION OF INTERESTS

None declared.

ACKNOWLEDGMENTS

None.

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