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Comparative Effectiveness of Smoking Cessation Treatments for Patients With Depression: A Systematic Review and Meta-analysis of the Evidence

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February 28, 2011

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Disclosure

This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the Durham VA Medical Center, Durham, NC, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

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VA Evidence-based Synthesis (ESP) Program Overview

- Sponsored by VA Office of R&D and HSR&D.
- Established to provide timely and accurate syntheses/reviews of healthcare topics identified by VA clinicians, managers and policy-makers, as they work to improve the health and healthcare of Veterans.
- Builds on staff and expertise already in place at the Evidence-based Practice Centers (EPC) designated by AHRQ. Four of these EPCs are also ESP Centers:
  - **Durham VA Medical Center;** VA Greater Los Angeles Health Care System; Portland VA Medical Center; and Minneapolis VA Medical Center.

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- Provides evidence syntheses on important clinical practice topics relevant to Veterans, and these reports help:
    - develop clinical policies informed by evidence,
    - the implementation of effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures, and
    - guide the direction for future research to address gaps in clinical knowledge.
- Broad topic nomination process – e.g. VACO, VISNs, field – facilitated by ESP Coordinating Center (Portland) through online process:

http://www.hsrd.research.va.gov/publications/esp/TopicNomination.cfm

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- Steering Committee representing research and operations (PCS, OQP, ONS, and VISN) provides oversight and guides program direction.
- Technical Advisory Panel (TAP)
  - Recruited for each topic to provide content expertise.
  - Guides topic development; refines the key questions.
  - Reviews data/draft report.
- External Peer Reviewers & Policy Partners
  - Reviews and comments on draft report
- Final reports posted on VA HSR&D website and disseminated widely through the VA.

http://www.hsrd.research.va.gov/publications/esp/reports.cfm

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Current Report

Comparative Effectiveness of Smoking Cessation Treatments for Patients With Depression: A Systematic Review and Meta-analysis of the Evidence (Nov, 2010)

Full-length report available on ESP website:

http://www.hsrd.research.va.gov/publications/esp/reports.cfm

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Acknowledgements

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Background

- Cigarette use is deadly but still common.
- Cigarette use is higher among Veterans with depression.
- Depression may be a barrier to smoking cessation.
- Smokers with depression can quit.

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Background

- Evidence-based smoking cessation intervention strategies:
  - ✓ Nicotine replacement therapy (NRT)
  - ✓ Some antidepressants (i.e., bupropion, nortriptyline)
  - ✓ Behavioral counseling (including proactive telephone counseling)
  - ✓ *Behavioral counseling + pharmacotherapy = gold standard care*

- Moderator effects?
  - Gender
  - Depression status
  - Content delivery sequencing

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METHODS

Key Questions

For patients with a history of a depressive disorder or current significant depressive symptoms:

- KQ1: What is the comparative effectiveness of different smoking cessation strategies on smoking abstinence rates?
- KQ2: Are there differential effects of smoking cessation strategies by depression status (i.e., history of MDD, current depressive symptoms, current MDD)?
- KQ3: Are there differential effects of smoking cessation strategies by gender?
- KQ4: Does treatment effectiveness differ by whether smoking cessation/depression treatments are delivered concurrently or sequentially?
- Key Question 5: What is the nature and frequency of adverse effects of smoking cessation treatments?

Study Eligibility

Study characteristic	Inclusion criteria
Study design	RCTs or a secondary data analysis from RCTs
Population	Adults age 18 and over with a history of a depressive disorder or current significant depressive symptoms
Interventions	Any patient-level smoking cessation strategies alone or in combination with other strategies
Comparators	Active comparators or control
Setting	Outpatient (e.g., mental health clinics, primary care) or delivered through remote communication technologies (e.g., telephone, Web)
Outcome	Smoking abstinence reported at ≥ 3 months postrandomization

Data Synthesis

- Pooled risk ratios with 95% CI
- Grouped studies as. . .
  - antidepressants
  - nicotine replacement therapy (NRT)
  - brief smoking cessation counseling
  - smoking cessation behavioral counseling
  - behavioral mood management therapy

- A priori moderator analysis by. . .
  - gender
  - depression status
  - treatment sequencing

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RESULTS

Literature Search and Study Characteristics Results

- Literature search:
  - Identified 884 titles; 92 full-text reviews
  - 23 included reports of 16 unique trials

- Study characteristics:
  - All US-based studies
  - 10 trials DID NOT used depression as inclusion criteria (used subgroup analysis from these trials)
  - Most tested combo treatment (e.g., counseling + pharmacotherapy)
  - Most common counseling type = CBT
  - One telephone-delivered study

Key Question 1 Results

For patients with a history of a depressive disorder or current significant depressive symptoms, what is the comparative effectiveness of different smoking cessation strategies on smoking abstinence rates?

Results: Nicotine Replacement Therapy

Study, year	Sample size (% depressed)	Intervention Arm	Comparator	Improved smoking cessation?
Kinnunen, 1996	269 (34% met criteria for depression)	Nicotine gum + one-time brief individual behavioral counseling	Placebo gum + one-time brief individual behavioral counseling	YES
Kinnunen, 2008	608 (32% met criteria for depression)	Nicotine gum + 9 brief in-person individual counseling sessions	Placebo gum + 9 brief in-person individual counseling sessions	YES
Hall, 1996	201 (22% MDD history positive)	Nicotine gum + 10 sessions of group CBT smoking cessation counseling or 10 session health education	Placebo gum + 10 sessions of group CBT smoking cessation counseling or 10 sessions health education	NO
Hall, 2006	322 (100% with current depression)	Transdermal nicotine patch (or bupropion if failed NRT) + staged motivational feedback + 6 sessions of individual CBT	Brief contact with self-help guide + list of referrals to smoking cessation programs and stop smoking guide	YES

Results: Antidepressant

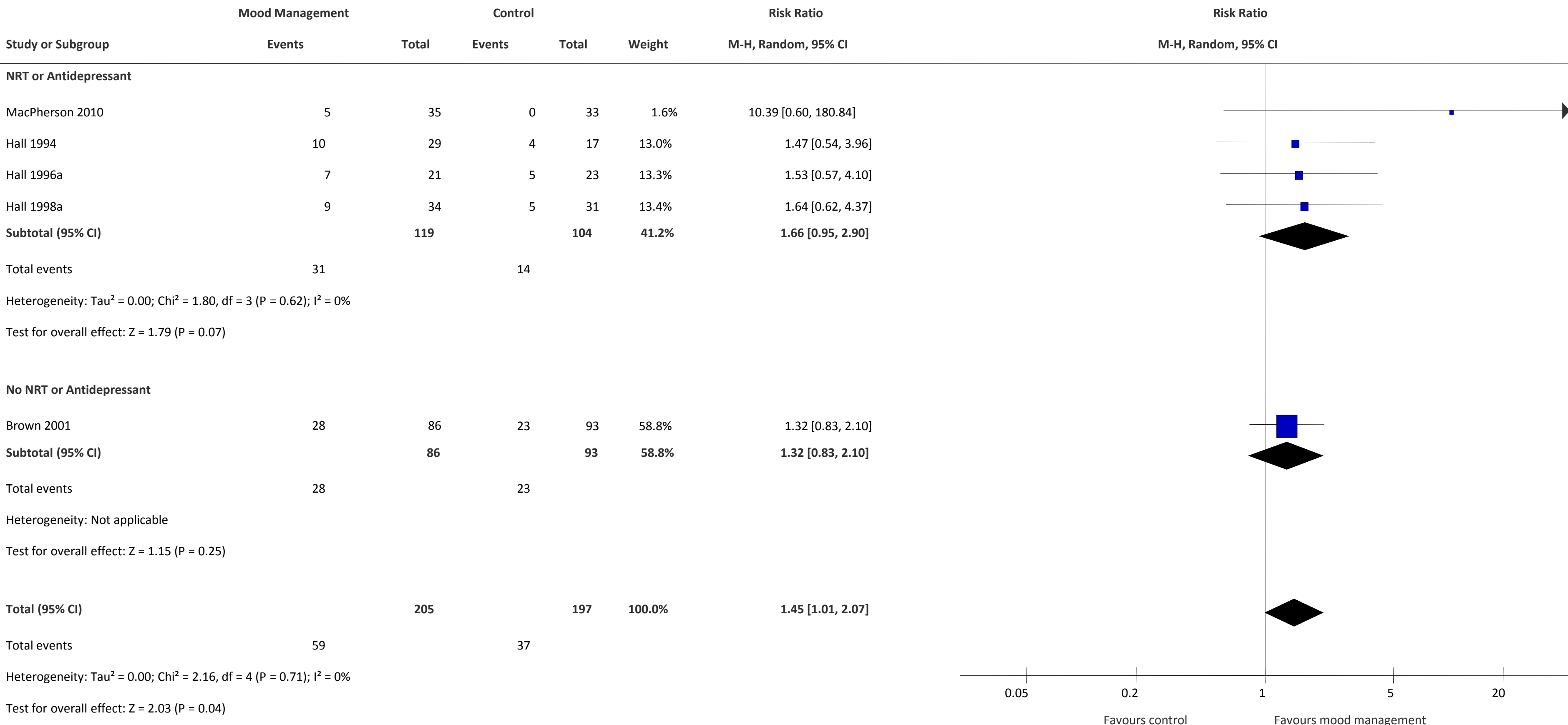
Risk of smoking abstinence at least 6 months after start of antidepressant therapy + behavioral counseling vs. placebo + behavioral counseling

Results: Antidepressants

Study, year	Sample size (% depressed)	Intervention Arm	Comparator	Improved smoking cessation?
Evins, 2008	199 (100% MDD history positive)	Bupropion + 13 group CBT smoking cessation counseling + NRT patch	Placebo + 13 group CBT smoking cessation counseling + NRT patch	NO
Saules, 2004	150 (20% MDD history positive)	Fluoxetine + 6 group CBT smoking cessation counseling + NRT patch	Placebo + 6 group CBT smoking cessation counseling + NRT patch	NO

Results: Mood Management Therapy

Risk of smoking abstinence at least 6 months after start of mood management therapy + cotreatment compared to active control



Study or Subgroup	Mood Management Events	Mood Management Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
NRT or Antidepressant						
MacPherson 2010	5	35	0	33	1.6%	10.39 [0.60, 180.84]
Hall 1994	10	29	4	17	13.0%	1.47 [0.54, 3.96]
Hall 1996a	7	21	5	23	13.3%	1.53 [0.57, 4.10]
Hall 1998a	9	34	5	31	13.4%	1.64 [0.62, 4.37]
Subtotal (95% CI)		**119**		**104**	**41.2%**	**1.66 [0.95, 2.90]**
Total events	31		14			
Heterogeneity: Tau² = 0.00; Chi² = 1.80, df = 3 (P = 0.62); I² = 0%						
Test for overall effect: Z = 1.79 (P = 0.07)						
No NRT or Antidepressant						
Brown 2001	28	86	23	93	58.8%	1.32 [0.83, 2.10]
Subtotal (95% CI)		**86**		**93**	**58.8%**	**1.32 [0.83, 2.10]**
Total events	28		23			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.15 (P = 0.25)						
Total (95% CI)		**205**		**197**	**100.0%**	**1.45 [1.01, 2.07]**
Total events	59		37			
Heterogeneity: Tau² = 0.00; Chi² = 2.16, df = 4 (P = 0.71); I² = 0%						
Test for overall effect: Z = 2.03 (P = 0.04)						

Results: Mood Management Therapy

Study, year	Sample size (% depressed)	Intervention Arm	Comparator	Improved smoking cessation?
Duffy, 2006	184 (35% depressed smokers)	9 to 11 session of combined smoking, depression, alcohol abuse telephone CBT + bupropion + NRT (if failed bupropion monotherapy in the past) OR NRT + paroxetine (if failed bupropion in the past for depression)	One-time behavioral counseling and referral to appropriate services for substance use/abuse and/or depression	Yes

Results: Other Strategies

Study, year	Sample size (% depressed)	Intervention Arm	Comparator	Improved smoking cessation?
Covey, 1999	80 (45% MDD history positive)	Naltrexone + 6 individual in-person behavioral counseling sessions	Placebo + 6 individual in-person behavioral counseling sessions	YES
Munoz, 1997	136 (78% MDE history positive)	Mailed smoking cessation guide + mood management guide	Mailed smoking cessation guide + mood management guide at 3 months delayed	YES
Vickers, 2009	60 (100% with current depression)	10 in-person individual exercise counseling sessions that include brief smoking cessation counseling + NRT	10 in-person individual health education sessions that include brief smoking cessation counseling + NRT	NO

Key Question 2 Results

For patients with a history of a depressive disorder or current significant depressive symptoms, are there differential effects of smoking cessation strategies by depression status (i.e., history of MDD, current depressive symptoms, current MDD)?

Results: Depression Status Moderation

Study, year	Intervention Arm	Comparator	Improved smoking cessation?
Evins, 2008	Bupropion + 13 group CBT smoking cessation counseling + NRT patch	Placebo + 13 group CBT smoking cessation counseling + NRT patch	MDD Hx positive (NO) Current depression (NO)
Munoz, 1997	Mailed smoking cessation guide + mood management guide	Mailed smoking cessation guide + mood management guide at 3 months delayed	MDD Hx positive (YES) Current MDD (NO)

Key Question 3 Results

For patients with a history of a depressive disorder or current significant depressive symptoms, are there differential effects of smoking cessation strategies by gender?

Key Question 4 Results

For patients with a history of a depressive disorder or current significant depressive symptoms, does treatment effectiveness differ by whether smoking cessation/depression treatments are delivered concurrently or sequentially?

Key Question 5 Results

For patients with a history of a depressive disorder or current significant depressive symptoms, what is the nature and frequency of adverse effects of smoking cessation treatments?

Adverse Effect Results

Study, year	Intervention	Adverse effects reported (% reported in intervention versus control)
Covey, 1999	Naltrexone + 6 individual in-person behavioral counseling sessions	Panic attack, malaise, sleeplessness, concentration difficulty, nausea and vomiting, disoriented and shaky, spaciness, dizzy, abdominal pain, lightheadedness, shortness of breath
Hall, 1998	5 group sessions of CBT mood management + 5 group sessions of smoking cessation counseling + nortriptyline	Dry mouth (78% vs 33%), lightheadedness (49% vs 22%) shaky hands (23% vs 11%) blurry vision (16% vs 6%)
Hayford, 1999	Bupropion + 11 brief in-person individual counseling sessions	Headache (29% vs 31-33%) insomnia (21% vs 30-35%) rhinitis (17% vs 10 to 12%) dry mouth (5% vs 13%) increased anxiety (11% vs 5-7%)
Kinnunen, 2008	Nicotine gum + 9 brief in-person individual counseling sessions	Heart palpitations, nausea, vomiting, dizziness, breathing difficulties, tongue blisters, damage to dental work, sore jaw
Saules, 2004	Fluoxetine + 6 group sessions of CBT smoking cessation counseling + NRT patch	Adverse effects not more common in intervention arms but did not list types

Limitations

- Broad intervention categories
- Few trials recruited depressed smokers
- Use of subgroup data
- Limited data on many KQs
- Few trials with VA users

Summary & Discussion

- Few trials
- Limited data on important treatment moderators
- Behavioral mood management therapy = small positive effect
- Antidepressants use = insufficient evidence
- NRT = small positive effect

Bottom line:
Patients with depression can quit smoking.

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Questions?

If you have further questions,
feel free to contact:

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The full report and cyberseminar presentation is available on the ESP website:

http://www.hsrd.research.va.gov/publications/esp/