



**Cochrane**  
**Library**

Cochrane Database of Systematic Reviews

## Lobeline for smoking cessation (Review)

Stead LF, Hughes JR

Stead LF, Hughes JR.  
Lobeline for smoking cessation.  
*Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No.: CD000124.  
DOI: [10.1002/14651858.CD000124.pub2](https://doi.org/10.1002/14651858.CD000124.pub2).

[www.cochranelibrary.com](http://www.cochranelibrary.com)

---

**Lobeline for smoking cessation (Review)**  
Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

**WILEY**

---

**TABLE OF CONTENTS**

ABSTRACT .....	1
PLAIN LANGUAGE SUMMARY .....	1
BACKGROUND .....	3
OBJECTIVES .....	3
METHODS .....	3
RESULTS .....	3
DISCUSSION .....	3
AUTHORS' CONCLUSIONS .....	4
REFERENCES .....	5
CHARACTERISTICS OF STUDIES .....	6
WHAT'S NEW .....	8
HISTORY .....	8
CONTRIBUTIONS OF AUTHORS .....	8
DECLARATIONS OF INTEREST .....	8
SOURCES OF SUPPORT .....	9
INDEX TERMS .....	9

[Intervention Review]

# Lobeline for smoking cessation

Lindsay F Stead<sup>1</sup>, John R Hughes<sup>2</sup>

<sup>1</sup>Department of Primary Care Health Sciences, University of Oxford, Oxford, UK. <sup>2</sup>Dept of Psychiatry, University of Vermont, Burlington, Vermont, USA

**Contact:** Lindsay F Stead, Department of Primary Care Health Sciences, University of Oxford, 23-38 Hythe Bridge Street, Oxford, OX1 2ET, UK. [lindsay.stead@phc.ox.ac.uk](mailto:lindsay.stead@phc.ox.ac.uk).

**Editorial group:** Cochrane Tobacco Addiction Group.

**Publication status and date:** New search for studies and content updated (no change to conclusions), published in Issue 2, 2012.

**Citation:** Stead LF, Hughes JR. Lobeline for smoking cessation. *Cochrane Database of Systematic Reviews* 2012, Issue 2. Art. No.: CD000124. DOI: [10.1002/14651858.CD000124.pub2](https://doi.org/10.1002/14651858.CD000124.pub2).

Copyright © 2012 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

## ABSTRACT

### Background

Lobeline is a partial nicotine agonist, which has been used in a variety of commercially available preparations to help stop smoking.

### Objectives

The objective of this review was to assess the effects of lobeline on long term smoking cessation.

### Search methods

We searched the Cochrane Tobacco Addiction Group trials register (most recent search December 2011).

### Selection criteria

Randomized trials comparing lobeline to placebo or an alternative therapeutic control, which reported smoking cessation with at least six months follow-up.

### Data collection and analysis

We extracted data in duplicate on the type of subjects, the dose and form of lobeline, the outcome measures, method of randomisation, and completeness of follow-up.

### Main results

We identified no trials meeting the full inclusion criteria including long term follow-up. One large trial failed to detect any effect on short-term abstinence.

### Authors' conclusions

There is no evidence available from long term trials that lobeline can aid smoking cessation, and the short-term evidence suggests there is no benefit

## PLAIN LANGUAGE SUMMARY

### Can lobeline help people to quit smoking

Lobeline is an alkaloid derived from the leaves of an Indian tobacco plant, and has been widely used in commercial smoking remedies. Its adverse effects include dizziness, nausea, and vomiting, and tablets and pastilles containing Lobeline may lead to throat irritation. The

---

review found no adequate long-term trials which could provide evidence that Lobeline can help people stop smoking. One large study with only six weeks follow-up did not detect any evidence of short-term benefit, suggesting that lobeline is not an effective treatment.

## BACKGROUND

Lobeline is an alkaloid derived from the leaves of an Indian tobacco plant (*Lobelia inflata*). It was synthesised in the early 1900s and classified as a partial nicotinic agonist. The first reported use in aiding smoking cessation was in the 1930s (Dorsey 1936). Since then it has been tested in a variety of doses and formulations, and has been quite widely used in proprietary smoking remedies.

Schwartz (Schwartz 1969) identified 16 studies or reviews of clinic success rates in which lobeline had been used. Few of these used placebo or other controls, or had follow-up beyond the end of treatment. Davison 1972 also reviewed the evidence and concluded that poor methodological quality prevented any conclusions on efficacy being drawn. In 1993 the FDA banned all OTC smoking cessation products in the United States, including lobeline, due to a lack of acceptable clinical efficacy data (FDA 1993). This led to renewed interest in investigating efficacy (Schneider 1996a; Glover 1998; Glover 2010).

The early use of high doses (8 mg tablets) of lobeline sulphate gave rise to considerable side effects; Wright (Wright 1937) cautioned against the drug's use because of the aversive gastric effects. Parenteral injection although reported as being particularly effective, caused dizziness, nausea and vomiting (Ejrup 1967). Even buffered tablets or flavoured pastilles may lead to local throat irritation, with the possibility that any short term efficacy could be due to a non-specific aversive effect.

## OBJECTIVES

To assess the current evidence for the effectiveness of lobeline in assisting long-term smoking cessation.

The hypothesis tested was that lobeline was more effective than placebo, or an alternative treatment, in achieving long-term smoking cessation.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Randomized studies using a placebo or an alternative therapeutic control.

#### Types of participants

Any smokers.

#### Types of interventions

Treatment with any form of lobeline.

#### Types of outcome measures

Smoking cessation, assessed at follow-up at least 6 months from start of treatment.

### Search methods for identification of studies

We searched the Tobacco Addiction Review Group Specialized Register of trials, using the free text or indexing term 'lobeline'. The most recent search of the Register was in December 2011, and included reports of trials indexed in MEDLINE to update 20110826, EMBASE to 2011 week 33, PsycINFO to 20110822 and the Cochrane

Central Register of Controlled trials to Issue 3, 2011. See the [Tobacco Addiction Group Module](#) for details of the search strategies for these databases. We also searched [clinicaltrials.gov](#) using the terms lobeline and smoking. Review bibliographies were searched for the original review.

## Data collection and analysis

In each study the strictest available criteria to define cessation would be used, with figures for sustained abstinence extracted in preference to point prevalence where both were presented. In studies which used biochemical validation of cessation, only those subjects meeting the criteria for biochemically confirmed abstinence would be regarded as having stopped smoking. Subjects in either group lost to follow-up would be regarded as being continuing smokers. Two reviewers would extract data independently. Statistical meta-analysis would be used to derive a typical Odds Ratio and its associated confidence intervals, using a fixed-effects model (Yusuf 1985).

## RESULTS

### Description of studies

No studies were found which met all criteria for inclusion. A number of early reports of the use of lobeline did not use any control groups. Of those which used a placebo, a number employed a cross over design with smoking behaviour assessed over days rather than weeks. Percentage reduction in number of cigarettes smoked was more commonly used as an outcome than complete abstinence. Few trials followed up beyond the end of treatment, and none for the required 6 month period.

### Risk of bias in included studies

Lack of long term follow-up was a reason for exclusion in all cases. A large number of the studies were not controlled. Where comparison was made with a placebo control or alternative treatment it was rarely clear that an appropriate method of randomization had been used.

### Effects of interventions

On the basis of the trials which have been published in the past sixty years there is no evidence that lobeline has any long term effect on smoking cessation.

## DISCUSSION

Trials with long-term follow-up using validated sustained abstinence are the gold standard for evaluating smoking cessation methods. Trials with short-term follow-up may overestimate both the overall abstinence rates and the size of any treatment effect.

Because short-term abstinence is not necessarily evidence of long-term cessation this review has not systematically synthesized and evaluated the evidence from short-term studies. However even these did not appear to provide consistent evidence that lobeline has an effect on smoking behaviour. A number of the early controlled short term trials concluded that lobeline had no effect on smoking; (Merry 1963; BTA 1963; Edwards 1964 A; Edwards 1964 B; Ross 1967; Leone 1968; Davison 1972).

More recent laboratory studies suggested that a formulation of lobeline with better bioavailability could be efficacious (Schneider

1996a; Schneider 1996b). This research included a pilot study comparing a sublingual lobeline tablet (7.5 mg, 9 times/day) with placebo for 6 weeks. Both groups received weekly individual counselling (Glover 1998). This study did not demonstrate short-term efficacy but there was a trend towards a benefit in more dependent participants and results were considered promising enough for a phase 3 trial. A multicentre study of sublingual lobeline sulfate tablets with 750 subjects was conducted by Dynagen in 1997 and identified as unpublished in previous versions of this review. It was published in 2010 (Glover 2010). There was no statistically significant difference in quitting between placebo (15% abstinent) and lobeline (17%) at 6 week follow-up. DynaGen discontinued its research programme, but it remains possible that formulations of lobeline for nasal, transdermal patch or transbuccal patch use may be further investigated by other companies. Since then, other nicotinic receptor partial agonists have been shown to be effective. Varenicline has been licensed widely for smoking cessation (Cahill 2011), whilst cytisine, like

lobeline a plant-derived compound, and used as a cessation medication in Eastern Europe, has now shown efficacy in one high quality trial with 12 month follow-up (West 2011).

## **AUTHORS' CONCLUSIONS**

### **Implications for practice**

There are no well conducted trials with long-term follow-up and one large short-term trial did not detect evidence of benefit. There is therefore no evidence that lobeline can aid smoking cessation.

### **Implications for research**

Given the established efficacy of nicotine replacement therapy (Stead 2008) and of partial nicotinic agonists (Cahill 2011), further trials are unlikely unless lobeline is shown to have potential advantages. In this case formulations that increase bioavailability and have good compliance would need to be developed.

## REFERENCES

**References to studies excluded from this review**
**Bachman 1964** {published data only}

Bachman DS. Group smoking deterrent therapy. *GP* 1964;**30**:86.

**Bartlett 1957** {published data only}

Bartlett WA, Whitehead RW. The effectiveness of meprobamate and lobeline as smoking deterrents. *Journal of Laboratory and Clinical Medicine* 1957;**50**(2):278-81.

**BTA 1963** {published data only}

British Tuberculosis Association Research Committee. Smoking deterrent study. *British Medical Journal* 1963;**2**:486-7.

**Davison 1972** {published data only}

Davison GC, Rosen RC. Lobeline and reduction of cigarette smoking. *Psychological Reports* 1972;**31**:443-56.

**Dorsey 1936** {published data only}

Dorsey JL. Control of the tobacco habit. *Annals of Internal Medicine* 1936;**10**:628-31.

**Edwards 1964 A** {published data only}

Edwards G. Double-Blind Trial of Lobeline in an Anti-Smoking Clinic. *Medical Officer* 1964;**112**:158-60.

**Edwards 1964 B** {published data only}

Edwards G. Hypnosis and lobeline in an Anti-Smoking Clinic. *Medical Officer* 1964;**111**:239-43.

**Ejrup 1959** {published data only}

Ejrup B. Follow-up of the material of smokers difficult to treat. *Svenska Läkartidningen* 1959;**56**:2254-62.

Ejrup B. Fortsatta forsok till avvanjning fran toback medelst injektions behandling. *Svenska Läkartidningen* 1959;**56**:1975-86.

**Ejrup 1967** {published data only}

Ejrup B. Report to American Cancer Society Conference of Experts on Ways to help people give up smoking. New York City. 19-20 Dec 1967.

**Farago 1968** {published data only}

Farago I. Results of a weaning cure of 1125 smokers. Contribution to the nicotine addiction problem [Ergebnisse der entwöhnungskuren von 1125 rauchern:beitrag zum nikotinsucht-problem]. *Schweizer Archiv fur Neurologie Neurochirurgie und Psychiatrie* 1968;**102**:167-89.

**Glover 1998** {published data only}

Glover ED, Leischow SJ, Rennard SI, Glover PN, Daughton D, Quiring JN, et al. A smoking cessation trial with lobeline sulfate: A pilot study. *American Journal of Health Behavior* 1998;**22**:62-74.

Schneider FH, Olsson TA. Clinical experience with lobeline as a smoking cessation agent. *Medicinal Chemistry Research* 1996;**6**:562-70.

**Glover 2010** {published data only}

DynaGen Inc. NicErase-SL multi-center phase 3 trial shows efficacy in one of three sites. Press Release 29 August 1997.

\* Glover ED, Rath JM, Sharma E, Glover PN, Laflin M, Tonnesen P, et al. A multicenter phase 3 trial of lobeline sulfate for smoking cessation. *American Journal of Health Behavior* 2010;**34**:101-9.

**Golledge 1965** {published data only}

Golledge AH. Influencing factors in ant-smoking clinics together with the results of a double blind trial of Lobidan. *Medical Officer* 1965;**114**:59-61.

**Graff 1966** {published data only}

Graff H, Hammet VO, Bash N, Fackler G, Yanovski A, Goldman A. Results of four antismoking methods. *Pennsylvania Medical Journal* 1966;**69**:86-9.

**Hoffstaedt 1964** {published data only}

Hoffstaedt EGW, Pearson RCM. The experimental smokers' advisory clinic Newcastle upon Tyne. *Medical Officer* 1964;**111**(31 Jan):59-60.

**Hoffstaedt 1965** {published data only}

Hoffstaedt EGW. The treatment of the unwilling smoker. A clinical approach. *Practitioner* 1965;**195**:794-8.

**Jacobs 1971** {published data only}

Jacobs MA, Spilken AZ, Norman MM, Wohlberg GW, Knapp PH. Interaction of personality and treatment conditions associated with success in a smoking control program. *Psychosomatic Medicine* 1971;**33**:545-56.

**Jochum 1961** {published data only}

Jochum K, Jost F. Nicotine addiction and its treatment. *Münchener Medizinische Wochenschrift* 1961;**103**:618-22.

**Kalyuzhny 1968** {published data only}

Kalyuzhny VV. The treatment of tobacco smoking by means of lobeline and the effect of lobeline on vegetative and vascular reactions. *Zh Nevropatol Psikhiatr* 1968;**68**:1864-70.

**Kaufman 1960** {published data only}

Kaufman H, Bensimon L. Tobacco withdrawal [Le sevrage du tabac]. *Vie Medicale* 1960;**41**:1139.

**Leone 1968** {published data only}

Leone LA, Musiker HR, Albala MM, McGurk W. A study of the effectiveness of the smoking deterrence clinic. *Rhode Island Medical Journal* 1968;**51**:247-257,260.

**London 1963** {published data only}

London SJ. Clinical evaluation of a new lobeline smoking deterrent. *Current Therapeutic Research* 1963;**5**(4):167-75.

**McChargue 2002** {published data only}

McChargue DE, Collins FL, Cohen LM. Effect of non-nicotinic moist snuff replacement and lobeline on withdrawal symptoms

during 48-h smokeless tobacco deprivation. *Nicotine & Tobacco Research* 2002;**4**(2):195-200.

**Merry 1963** {published data only}

Merry J, Preston G. The effect of buffered lobeline sulphate on cigarette smoking. *Practitioner* 1963;**190**:628-31.

**Perlstein 1964** {published data only}

Perlstein IB. Smoking deterrent therapy in private practice. The first M.R. Thompson Symposium on recent advances in the medical aspects of smoking. New York: Matthew Publishing Co, 1964:40-5.

**Rapp 1955** {published data only}

Rapp GW, Olen AA. A critical evaluation of a lobeline based smoking deterrent. *American Journal of Medical Science* 1955;**230**:9-14.

**Rapp 1959** {published data only}

Rapp GW, Dusza BT, Blanchet L. Absorption and utility of lobeline as a smoking deterrent. *American Journal of Medical Science* 1959;**237**:287-92.

**Rosenberg 1959** {published data only}

Rosenberg A. Attempt at stopping the tobacco habit. *Ugeskrift for Laeger* 1959;**121**:881-6.

**Rosnick 1965** {published data only}

Rosnick MJ. The smoking deterrent effect of a new lobeline dosage form. *Journal of the Florida Medical Association* 1965;**52**:27-30.

**Ross 1967** {published data only}

Ross CA. Smoking withdrawal research clinics. *American Journal of Public Health* 1967;**57**:677-81.

**Schneider 1996a** {published data only}

Schneider FH, Olsson TA. Clinical experience with lobeline as a smoking cessation agent. *Medicinal Chemistry Research* 1996;**6**:562-70.

**Schneider 1996b** {published data only}

Schneider FH, Mione PJ, Raheman FS, Phillips BM, Quiring JN. Reduction of tobacco withdrawal symptoms by sublingual lobeline sulfate. *American Journal of Health Behavior* 1996;**20**:346-63.

**Scott 1962** {published data only}

Scott GW, Cox AGC, MacLean KS, Price TML, Southwell N. Buffered lobeline as a smoking deterrent. *Lancet* 1962;**279**(7219):54-5.

**Swartz 1964** {published data only}

Swartz H, Cohen A. Clinical evaluation of SmoKurb as a smoking deterrent. *Current Therapeutic Research* 1964;**6**(4):290-6.

**Wright 1937** {published data only}

Wright IS, Littauer D. Lobeline sulphate: its pharmacology and use in the treatment of the tobacco habit. *JAMA* 1937;**109**:649-654.

## Additional references

**Cahill 2011**

Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database of Systematic Reviews. *Cochrane Database of Systematic Reviews* 2011, Issue 2. [DOI: [10.1002/14651858.CD006103.pub5](https://doi.org/10.1002/14651858.CD006103.pub5)]

**FDA 1993**

Department of Health and Human Services, Food, Drug Administration. Smoking deterrent drug products for Over-the-Counter human use. FR 31236 1 June 1993; Vol. 58, issue 103.

**Schwartz 1969**

Schwartz JL. A critical review and evaluation of smoking control methods. *Public Health Reports* 1969;**84**:483-506.

**Stead 2008**

Stead LF, Perera R, Bullen C, Mant D, Lancaster T. Nicotine replacement therapy for smoking cessation. *Cochrane Database of Systematic Reviews* 2008, Issue 1. [DOI: [10.1002/14651858.CD000146.pub3](https://doi.org/10.1002/14651858.CD000146.pub3)]

**West 2011**

West R, Zatonski W, Cedzynska M, Lewandowska D, Pazik J, Aveyard P, et al. Placebo-controlled trial of cytidine for smoking cessation. 2011. *New England Journal of Medicine* 2011;**365**:1193-1200.

**Yusuf 1985**

Yusuf S, Peto R, Lewis J, Collins R, Sleight P. Beta blockade during and after myocardial infarction: an overview of the randomized trials. *Progress in Cardiovascular Disease* 1985;**27**(5):335-71.

\* Indicates the major publication for the study

## CHARACTERISTICS OF STUDIES

### Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
<a href="#">Bachman 1964</a>	Double blind crossover evaluation of Nikoban.

### Lobeline for smoking cessation (Review)



Study	Reason for exclusion
<a href="#">Bartlett 1957</a>	Crossover trial comparing lobeline, meprobamate and placebo. Smokers not attempting to cut down.
<a href="#">BTA 1963</a>	Only six week follow-up
<a href="#">Davison 1972</a>	No follow-up after 4 weeks treatment.
<a href="#">Dorsey 1936</a>	Not controlled
<a href="#">Edwards 1964 A</a>	Double blind trial, follow-up only 3 months after 4 weeks of treatment
<a href="#">Edwards 1964 B</a>	Subjects alternated to lobeline or hypnosis. Only 3 month follow-up after treatment.
<a href="#">Ejrup 1959</a>	Not controlled. Used lobeline injections in a smoking clinic.
<a href="#">Ejrup 1967</a>	Not controlled. Used lobeline injections in smoking clinics.
<a href="#">Farago 1968</a>	Not controlled. Cited by <a href="#">Schneider 1996a</a> for use of parenteral lobeline.
<a href="#">Glover 1998</a>	No follow-up after 6 weeks of treatment.
<a href="#">Glover 2010</a>	No follow-up after 6 weeks of treatment.
<a href="#">Golledge 1965</a>	Only 28 day follow-up.
<a href="#">Graff 1966</a>	Only 3 month follow-up.
<a href="#">Hoffstaedt 1964</a>	No control group. Lobeline, hydroxyzine and discussion in a smoking clinic.
<a href="#">Hoffstaedt 1965</a>	No control group. Lobeline, hydroxyzine and discussion in a smoking clinic.
<a href="#">Jacobs 1971</a>	Only 10 week follow-up.
<a href="#">Jochum 1961</a>	Lobeline compared with psychotherapy. No follow-up.
<a href="#">Kalyuzhny 1968</a>	No long term follow-up. Cited by <a href="#">Schneider 1996a</a> for use of parenteral lobeline.
<a href="#">Kaufman 1960</a>	Not controlled.
<a href="#">Leone 1968</a>	Describes a number of clinics. Outcomes not reported for lobeline and placebo separately. 6 week follow-up.
<a href="#">London 1963</a>	Controlled trial of 0.5 mg pastilles. No follow-up after 4 weeks treatment
<a href="#">McChargue 2002</a>	Controlled trial of lobeline and moist snuff replacement with placebos over four weeks (one week for each condition). Follow-up for each measured 48 hours later.
<a href="#">Merry 1963</a>	Controlled trial of lobeline or placebo after failure to quit with one week without medication and one week on placebo. No post treatment follow-up.
<a href="#">Perlstein 1964</a>	No post-treatment follow-up reported
<a href="#">Rapp 1955</a>	Crossover trial of lobeline and placebo. Smoking behaviour recorded for one week on each.
<a href="#">Rapp 1959</a>	Crossover study of lobeline sulphate in capsules, Bantron in capsules or starch placebo.

Study	Reason for exclusion
<a href="#">Rosenberg 1959</a>	Controlled trial, no long term follow-up data reported.
<a href="#">Rosnick 1965</a>	No long term follow-up.
<a href="#">Ross 1967</a>	Long term quit rates not reported by treatment group.
<a href="#">Schneider 1996a</a>	Short follow-up. See <a href="#">Glover 1998</a> for full study report.
<a href="#">Schneider 1996b</a>	Not a cessation study; effect of lobeline on withdrawal symptoms after overnight abstinence
<a href="#">Scott 1962</a>	Crossover study with no long term follow-up.
<a href="#">Swartz 1964</a>	Not controlled.
<a href="#">Wright 1937</a>	Not controlled.

## WHAT'S NEW

Date	Event	Description
4 January 2012	New search has been performed	One new excluded study added
3 January 2012	New citation required but conclusions have not changed	Excluded study described in discussion. Evidence for absence of effect is strengthened

## HISTORY

Protocol first published: Issue 3, 1997

Review first published: Issue 3, 1997

Date	Event	Description
8 January 2009	New search has been performed	No new trials found
28 October 2008	Amended	Converted to new review format.
27 April 2006	New search has been performed	Searches rerun, no new studies
19 May 2003	New search has been performed	One reference added to excluded studies list

## CONTRIBUTIONS OF AUTHORS

LS and JH conceived the review; both extracted data, and collaborated on original text and subsequent updates

## DECLARATIONS OF INTEREST

JH has received consulting fees from several for-profit and nonprofit organizations that provide smoking cessation medications and services.

---

## SOURCES OF SUPPORT

### Internal sources

- Department of Primary Health Care, University of Oxford, UK.
- National School for Health Research School for Primary Care Research, UK.

### External sources

- NHS National Institute for Health Research, NIHR Evaluation Trials and Studies Coordinating Centre, UK.

## INDEX TERMS

### Medical Subject Headings (MeSH)

\*Smoking Prevention; Lobeline [\*therapeutic use]; Nicotinic Antagonists [\*therapeutic use]; Smoking Cessation [\*methods]

### MeSH check words

Humans