Ontario Health Technology Assessment Series 2010; Vol. 10, No. 1

Population-Based Smoking Cessation Strategies

A Summary of a Select Group of Evidence-Based Reviews

Presented to the Ontario Health Technology Advisory Committee in September, 2009

January 2010

Ontario

Medical Advisory Secretariat
Ministry of Health and Long-Term Care

Suggested Citation

This report should be cited as follows:

Medical Advisory Secretariat. Population-based smoking cessation strategies: a summary of a select group of evidence-based reviews. *Ontario Health Technology Assessment Series* 2010;10(1).

Permission Requests

All inquiries regarding permission to reproduce any content in the *Ontario Health Technology Assessment Series* should be directed to MASinfo.moh@ontario.ca.

How to Obtain Issues in the Ontario Health Technology Assessment Series

All reports in the *Ontario Health Technology Assessment Series* are freely available in PDF format at the following URL: www.health.gov.on.ca/ohtas.

Print copies can be obtained by contacting MASinfo.moh@ontario.ca.

Conflict of Interest Statement

All analyses in the Ontario Health Technology Assessment Series are impartial and subject to a systematic evidence-based assessment process. There are no competing interests or conflicts of interest to declare.

Peer Review

All Medical Advisory Secretariat analyses are subject to external expert peer review. Additionally, the public consultation process is also available to individuals wishing to comment on an analysis prior to finalization. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Contact Information

The Medical Advisory Secretariat
Ministry of Health and Long-Term Care
20 Dundas Street West, 10th floor
Toronto, Ontario
CANADA
M5G 2C2
Email: MASinfo.moh@ontario.ca
Telephone: 416-314-1092

ISSN 1915-7398 (Online)
ISBN 978-1-4435-1555-9 (PDF)

About the Medical Advisory Secretariat

The Medical Advisory Secretariat is part of the Ontario Ministry of Health and Long-Term Care. The mandate of the Medical Advisory Secretariat is to provide evidence-based policy advice on the coordinated uptake of health services and new health technologies in Ontario to the Ministry of Health and Long-Term Care and to the healthcare system. The aim is to ensure that residents of Ontario have access to the best available new health technologies that will improve patient outcomes.

The Medical Advisory Secretariat also provides a secretariat function and evidence-based health technology policy analysis for review by the Ontario Health Technology Advisory Committee (OHTAC).

The Medical Advisory Secretariat conducts systematic reviews of scientific evidence and consultations with experts in the health care services community to produce the *Ontario Health Technology Assessment Series*.

About the Ontario Health Technology Assessment Series

To conduct its comprehensive analyses, the Medical Advisory Secretariat systematically reviews available scientific literature, collaborates with partners across relevant government branches, and consults with clinical and other external experts and manufacturers, and solicits any necessary advice to gather information. The Medical Advisory Secretariat makes every effort to ensure that all relevant research, nationally and internationally, is included in the systematic literature reviews conducted.

The information gathered is the foundation of the evidence to determine if a technology is effective and safe for use in a particular clinical population or setting. Information is collected to understand how a new technology fits within current practice and treatment alternatives. Details of the technology's diffusion into current practice and input from practising medical experts and industry add important information to the review of the provision and delivery of the health technology in Ontario. Information concerning the health benefits; economic and human resources; and ethical, regulatory, social and legal issues relating to the technology assist policy makers to make timely and relevant decisions to optimize patient outcomes.

If you are aware of any current additional evidence to inform an existing evidence-based analysis, please contact the Medical Advisory Secretariat: MASinfo.moh@ontario.ca. The public consultation process is also available to individuals wishing to comment on an analysis prior to publication. For more information, please visit http://www.health.gov.on.ca/english/providers/program/ohtac/public_engage_overview.html.

Table of Contents

List of Tables

List of Abbreviations

CDTQ	Cut down to quit
CEA	Cost-effectiveness analysis
CI	Confidence interval(s)
CVD	Cardiovascular disease
HTA	Health Technology Assessment
MAS	Medical Advisory Secretariat
MHP	Ministry of Health Promotion
NRT	Nicotine replacement therapy
OHIP	Ontario Health Insurance Plan
OHTAC	Ontario Health Technology Advisory Committee
OR	Odds ratio
RCT	Randomized controlled trial
RR	Relative risk
SSRI	Selective serotonin reuptake inhibitor

Executive Summary

Objective

The objective of this report was to provide the Ministry of Health Promotion (MHP) with a summary of existing evidence-based reviews of the clinical and economic outcomes of population-based smoking cessation strategies.

Background

Tobacco use is the leading cause of preventable disease and death in Ontario, linked to approximately 13,000 avoidable premature deaths annually – the vast majority of these are attributable to cancer, cardiovascular disease, and chronic obstructive lung disease. (1) In Ontario, tobacco related health care costs amount to $6.1 billion annually, or about $502 per person (including non-smokers) and account for 1.4% of the provincial domestic product. (2) In 2007, there were approximately 1.7 to 1.9 million smokers in Ontario with two-thirds of these intending to quit in the next six months and one-third wanting to quit within 30 days. (3) In 2007/2008, Ontario invested $15 million in cessation programs, services and training. (4) In June 2009, the Ministry of Health Promotion (MHP) requested that MAS provide a summary of the evidence base surrounding population-based smoking cessation strategies.

Project Scope

The MAS and the MHP agreed that the project would consist of a clinical and economic summary of the evidence surrounding nine population-based strategies for smoking cessation including:

1. Mass media interventions
2. Telephone counselling
3. Post-secondary smoking cessation programs (colleges/universities)
4. Community-wide stop-smoking contests (i.e. Quit and Win)
5. Community interventions
6. Physician advice to quit
7. Nursing interventions for smoking cessation
8. Hospital-based interventions for smoking cessation
9. Pharmacotherapies for smoking cessation, specifically:
    a) Nicotine replacement therapies
    b) Antidepressants
    c) Anxiolytic drugs
    d) Opioid antagonists
    e) Clonidine
    f) Nicotine receptor partial agonists

Reviews examining interventions for Cut Down to Quit (CDTQ) or harm reduction were not included in this review. In addition, reviews examining individual-level smoking cessation strategies (i.e. self-help interventions, counselling, etc.), web-based smoking cessation interventions, and smoking cessation strategies for special population groups outside of those identified from reviews included in this analysis were excluded from the scope. Information on cessation programs or strategies in other provinces or an evaluation of current population-based programs in Ontario was also not included in the scope.

Status in Ontario

In 2005, the McGuinty government launched the Smoke-Free Ontario Strategy, focusing on initiatives aimed at young people to encourage them not to smoke, protection from exposure to second-hand smoke, and programs to help smokers quit. There are currently many smoking cessation programs funded across the province and in 2007/2008, Ontario invested $15 million in cessation programs, services and training. Ontario Health Insurance Plan (OHIP) fee codes for physician advice to quit also exist.

Evidence-Based Analysis

Research Question

What are the efficacy and cost-effectiveness of the selected population-based strategies for smoking cessation?

Literature Search

A preliminary scan of Medline was conducted to identify major systematic reviews, meta-analyses, and health technology assessments (HTAs) in the area of smoking cessation. Based on the availability of a number of Cochrane Reviews on the topic of smoking cessation, a more systematic search of the literature was not conducted. For the economic analysis, a literature search was conducted of relevant databases for recently published article reviews, HTAs, and Cochrane Reviews of the nine identified population-based smoking cessation strategies. This analysis is limited as it is a summary of existing reviews and not a systematic review.

Outcomes of Interest

The primary outcome of interest for the clinical summary was abstinence from smoking at 6 months follow up; additional outcomes were examined where available. The primary outcomes of interest for the economic analysis were cost-effectiveness ratios.

Summary of Findings

1. The evidence suggests that pharmacotherapy, physician advice to quit, nursing interventions, hospital-based interventions, and proactive telephone counselling are effective and cost-effective in the short-term.
2. There is poor quality data around other population-based smoking cessation strategies including mass media campaigns, community interventions, quit and win contests, access to ‘quitlines’, and interventions for university and college campuses, making evaluation of their effectiveness and cost-effectiveness difficult.
3. Based on pooled summary estimates of effect and safety data, the most effective strategies are varenicline, buproprion, and nicotine replacement therapies, followed by physician advice to quit and nursing interventions (in non-hospitalized smokers without cardiovascular disease).

Background

Objective of Analysis

The objective of this report was to provide the Ministry of Health Promotion (MHP) with a summary of existing evidence-based reviews of the clinical and economic outcomes of population-based smoking cessation strategies.

Background

Tobacco use is the leading cause of preventable disease and death in Ontario, linked to approximately 13,000 avoidable premature deaths annually – the vast majority of these are attributable to cancer, cardiovascular disease, and chronic obstructive lung disease. (1) In Ontario, tobacco related health care costs amount to $6.1 billion annually, or about $502 per person (including non-smokers) and account for 1.4% of the provincial domestic product. (2) In 2007, there were approximately 1.7 to 1.9 million smokers in Ontario with two-thirds of these smokers intending to quit within the next six months and one-third wanting to quit within 30 days. (3) In 2007/2008, Ontario invested $15 million in cessation programs, services, and training (4). In June 2009, the MHP requested that MAS provide a summary of the evidence surrounding population-based smoking cessation strategies.

Project Scope

The MAS and the MHP agreed that the project scope should cover a clinical and economic summary of the evidence surrounding nine population-based strategies for smoking cessation including:

1. Mass media interventions
2. Telephone counselling
3. Post-secondary smoking cessation programs (colleges/universities)
4. Community-wide stop-smoking contests (i.e. Quit and Win)
5. Community interventions
6. Physician advice to quit
7. Nursing interventions for smoking cessation
8. Hospital-based interventions for smoking cessation
9. Pharmacotherapies for smoking cessation, specifically:
    a) Nicotine replacement therapies
    b) Antidepressants
    c) Anxiolytic drugs
    d) Opioid antagonists
    e) Clonidine
    f) Nicotine receptor partial agonists

Reviews examining interventions for Cut Down to Quit (CDTQ) or harm reduction were not included in this review. In addition, reviews examining individual-level smoking cessation strategies (i.e. counselling, self-help interventions etc.), web-based smoking cessation interventions, and smoking cessation strategies for special population groups outside of those identified in existing reviews included in this analysis were excluded from the scope. Information on cessation programs or strategies in other provinces or evaluations of current population-based programs in Ontario were also not included in the scope.

Status in Ontario

In 2005, the McGuinty government launched the Smoke-Free Ontario Strategy focusing on initiatives aimed at young people to encourage them not to smoke, protection from exposure to second-hand smoke, and programs to help smokers quit. There are currently many smoking cessation programs funded across the province and in 2007/2008, Ontario invested $15 million in cessation programs, services and training. OHIP fee codes for physician advice to quit also exist.

Evidence-Based Analysis

Research Question

What are the efficacy and cost-effectiveness of the selected population-based strategies for smoking cessation?

Methods

Literature Search

A preliminary scan of Medline was conducted to identify major systematic reviews, meta-analyses, and health technology assessments (HTAs) in the area of smoking cessation. Based on the availability of a number of Cochrane Reviews on the topic of smoking cessation, a more systematic search of the literature was not conducted. For the economic analysis, a literature search was conducted of relevant databases (see Appendix 1) for recently published article reviews, HTAs, and Cochrane Reviews of the nine identified population-based smoking cessation strategies. This analysis is limited as it is a summary of existing reviews and not a systematic review.

Outcomes of Interest

The primary outcome of interest for the clinical summary was abstinence from smoking at 6 months follow up; additional outcomes were examined where available. The primary outcomes of interest for the economic analysis were cost-effectiveness ratios.

Statistical Analysis

We reported on meta-analyses from the systematic reviews. Since relative risks are preferred to odds ratios in reporting of smoking cessation trials, all odds ratios in the pooled analyses were converted to relative risks. New forest plots were then generated and results reported as relative risks. Although the preferred outcome in these trials is sustained and biochemically validated abstinence (versus point prevalence and/or self-reported quitting), many of the identified studies did not use this outcome and/or it was unclear whether sustained abstinence was required. Sensitivity analyses were, however, completed in all trials examining whether poorer quality trials impacted the effect size.

Quality of Evidence

The quality of evidence was summarized and discussed for each of the identified reviews. The limitations of the individual studies are discussed, as well as their relevance to the study findings and estimates of effect for various interventions.

Results of Evidence-Based Analysis

Fifteen systematic reviews and/or meta-analyses on population-based smoking cessation were identified in the literature, as summarized in Table 1. Each of these studies examined one or more of the nine different strategies of interest in this report. The summary of results for each of these strategies follows below.

Table 1: Systematic reviews and meta-analyses used for this report

Review Type	Authors	Topic	Included Research
Systematic Review	Murphy-Hoefer R, Griffith R, Pederson L, Crossett L, Iyer S, Hiller M (5)	Reducing Tobacco Use in Colleges and Universities	Up to Dec. 2003
Cochrane	Rigotti N, Munafo' MR, Stead LF (6)	Interventions for smoking cessation in hospitalised patients	Up to May 2007
Cochrane	Secker-Walker RH, Gnich W, Platt S, Lancaster T (7)	Community interventions for reducing smoking among adults	Up to Jan. 2006
Cochrane	Cahill K, Perera R (8)	Quit and win contests for smoking cessation	Up to Nov. 2007
Cochrane	Cahill K, Stead LF, Lancaster T (9)	Nicotine receptor partial agonists for smoking cessation	Up to Mar. 2008
Cochrane	Hughes JR, Stead LF, Lancaster T (10)	Axiolytic drugs	Up to Apr. 2007
Cochrane	David S, Lancaster T, Stead LF, Evins AE (11)	Opioid antagonists	Up to Mar. 2006
Cochrane	Stead LF, Perera R, Bullen C, Mant D, Lancaster T (12)	Nicotine Replacement Therapy	Up to July 2007
Cochrane	Stead LF, Bergson G, Lancaster T (13)	Physician advice to quit	Up to Sep. 2007
Cochrane	Gourlay SG, Stead LF, Benowitz N (14)	Clonidine for smoking cessation	June 2008
Cochrane	Hughes JR, Stead LF, Lancaster T (15)	Antidepressants for smoking cessation	Oct. 2006
Cochrane	Bala M, Strzeszynski L, Cahill K (16)	Mass Media Interventions	Mar. 2007
Cochrane	Stead LF, Perera R, Lancaster T (17)	Telephone Counselling/ Quitlines	Up to Dec. 2005
Cochrane	Rice VH and Stead LF (18)	Nursing Interventions	Up to July 2007

1. Mass Media Campaigns

The most recent systematic review identified from the literature was completed by Cochrane. (16) The objective of the review was to assess the effectiveness of mass media interventions in reducing smoking among adults. The following is a summary of the review.

Methods

The studies examined in the review were controlled trials, either randomized or non-randomized, that allocated communities, regions or states to intervention or control conditions. The intervention consisted of mass media defined 'as channels of communication intended for a large audience which do not rely on person-to-person contact.' The specific types of media included were: television, radio, newspapers, billboards, posters leaflets or booklets, all of which had to have the promotion of smoking cessation as their primary message. The study population included adult smokers (aged 25 or older) and the primary outcome measure was tobacco reduction, as assessed by prevalence and quit rates. Tobacco reduction was used as a secondary outcome and measured through changes in cigarette consumption (purchased or smoked), prevalence of daily smoking, and quit attempts. Outcomes were ideally measured at longest follow up, which was at least 6 months from beginning of the intervention. Biochemical validation of smoking cessation was not required for the inclusion of a study into this review. Intermediate and process measures, such as attitudes to smoking and maintenance of programmes after the interventions, were also examined. A meta-analysis was not performed due to the heterogeneity among the studies.

Results

Eleven studies were included in the review, the majority (8/11) of which had strong designs that employed a combination of TV, radio, print media, and billboard and/or poster advertising. Three of the studies, however, had methodological limitations including poor outcome measurement or interference by other concurrent tobacco control interventions. Study populations varied with some targeting only men, two including only male Vietnamese immigrants in the USA, and two studies that had state-wide campaigns targeting adults, adolescents, and the general population. Nine campaigns aimed to change smoking behaviour while two sought to reduce cardiovascular risk factors. Two were also part of wider tobacco control programmes.

Smoking behaviour was ascertained using a variety of outcomes and reported differently across studies. Nine campaigns reported smoking prevalence and in seven of these, it was the primary study outcome. Intermediate measures and process measures were reported in some studies, although due to the heterogeneity of the campaigns, it's difficult to draw conclusions from this data. Significant decreases were observed in both state-wide campaigns (as compared to the rest of US), but these were each part of wider tobacco control programmes. Of the remaining seven studies, three showed some positive effects on prevalence, either within their whole study populations or within particular subgroups.

Seven studies also reported quit and/or abstinence rates with four of these achieving some positive effect on increasing quit rates and three achieving a statistically significant decrease in cigarette consumption. The results of these studies did, however, show heterogeneity in outcome ascertainment, quality of reporting, and the subgroups examined. Furthermore, two of the studies achieving significant decreases were the state-wide campaigns, which were part of larger tobacco-wide control programmes.

In the five studies that reported quit attempts, data assessment and reporting was poor. Of note, two found no significant differences between intervention and control groups and one study only assessed quit attempts among continuing smokers. The two state-wide campaigns assessed quit attempts only in the intervention community and one failed to show a significant difference, while the other did not use statistical methods to compare groups.

Limitations

The authors noted that mass media campaigns are difficult to evaluate since their evaluation requires large sample sizes to detect small differences in the population. Furthermore, it is difficult to examine the specific contribution of a mass media campaign to the outcomes observed as often other tobacco control initiatives are taking place concurrently. Further, the studies included in this review were not randomized controlled trials (RCTs) and none could test a mass media intervention in isolation. Many of the studies included other components such as quit lines, and some compared populations receiving a mass media campaign to a control receiving a mass media campaign and a community intervention introducing confounding factor, thus making direct comparison difficult. Poor reporting of the study population demographics was evident and comparisons between intervention and control communities were only completed in five of the 11 studies, introducing uncertainty in any observed effects. Drop-outs, missing data, and participants lost to follow up were also poorly reported, especially in most of the positive studies. The studies also varied with respect to definitions of smoker, ex-smoker and quitter making it difficult to compare results between studies. Differences by age, gender, ethnicity and education were also difficult to ascertain based on the quality of data.

Authors' Conclusions

- *Tobacco control programmes that include mass media campaigns may change smoking behaviour in adults, but the evidence comes from studies of variable quality and scale. The specific contribution of the mass media component is unclear.*
- *The duration and intensity of an intervention may affect its impact on smoking behaviour, but evaluations need to extend for long enough to detect lasting changes, and to allow for confounders and for secular trends.*
- *No consistent relationship was observed between campaign effectiveness and age, education, ethnicity or gender.*

2. Telephone counselling for smoking cessation

A systematic review by Cochrane evaluated the effect of proactive and reactive telephone support to help smokers quit. (17) The following is a summary of the review.

Methods

Studies for the review were selected if they were RCTs or quasi-RCTs that offered proactive or reactive telephone counselling to aid smoking cessation to either smokers or recent quitters. The primary outcome of the trials was abstinence from smoking after at least 6 months follow up from the start of the intervention expressed as an odds ratio (MAS converted these figures to 'Relative Risks', or RRs). Studies excluded from the review were those that exclusively recruited quitters or studies that examined telephone counselling as an intervention for relapse. Studies focused on teens and pregnant women were included but were considered a potential source of heterogeneity in the analysis. Meta-analysis was performed where appropriate using a fixed-effect model.

Results

Forty-eight studies were identified in the review, which included a total of over 36, 000 participants. The intervention in the majority of trials was proactive counselling calls with the number of calls ranging from 1 to 12 over weeks or months (with an average duration of 10-20 minutes per call). Counselling was most commonly provided by professional counsellors or trained healthcare professionals.

As summarized in Table 2, the authors identified three broad trial categories:

a) those assessing the effect of providing access to a helpline (2 trials);

b) those of interventions for smokers who contacted a helpline (10 trials); and

c) those that offered support proactively in other settings (not initiated by calls to quitlines) (29 trials)

Seven trials did not fit into these categories and thus were assessed separately (Table 3).

Table 2: This table has subgroups separated by lightly shaded bars

Intervention	No. of studies	RR (95% CI) of Smoking Cessation
Trials providing access to a helpline		
	2	Not estimable
Interventions for people calling quitlines		
Comparison of different support during a single call*	2	1.10 (0.86, 1.42)
Effect of additional proactive calls	8	1.36 (1.23, 1.50)
Interventions of proactive counselling, not initiated by calls to quitlines		
All studies	29	1.29 (1.19, 1.40)
Baseline Support	29	1.29 (1.19, 1.40)
Intensity	29	1.29 (1.19, 1.40)
≤2 sessions	7	1.00 (0.83, 1.20)
3-6 sessions	19	1.31 (1.19, 1.45)
≥7 sessions	3	1.88 (1.42, 2.48)
Motivation	29	1.29 (1.19, 1.40)
Selected for motivation	10	1.51 (1.32, 1.71)
Not selected for motivation	19	1.16 (1.04, 1.29)

RR refers to relative risk; CI refers to confidence interval

* One study compared a counselling approach based on the stage of change model vs. provision of general information; one study compared counselling and materials to standard advice and materials

Studies examining access to a helpline could not be pooled and included different intervention components. One study found a statistically significant increase in quit rates while the other found no significant differences in quit rates between the intervention and control group. There was a statistically significant effect of additional proactive calls to provision of materials or brief counselling at a single call demonstrated by an RR of 1.63 (95% CI: 1.23, 1.50) for smoking cessation at 6 months. Interventions of proactive counselling were also found to have a modest benefit on smoking cessation at 6 months (RR 1.29; 95% CI: 1.19, 1.40). The observed benefit was greater in studies where patients were selected for motivation and the intensity of calls was greater. Seven studies considered too heterogeneous were not included in the pooled analysis (see table 3). Three of the seven studies showed an increase in quit rates or sustained abstinence while the remaining studies found no significant effects of the interventions on smoking cessation outcomes.

Table 3: Description of seven studies not included in pooled analysis

Study	Group 1	Group 2	Conclusion
Miller 1997	Hospital based intervention followed by a single call	Intensive intervention (up to 4 calls) from hospital discharge	More intensive intervention increased continuous 1-year quit rate from 14% to 19% (P=0.05)
Swan 2003	Single call (behavioural support) + Bupropion	4 brief calls (behavioural support) + Bupropion	OR 1.46, 95% CI: 1.17, 1.82 in favour of more intensive intervention
Mermelstein 2003	Non-specific support for smokers who had completed a group cessation course	Enhanced support for smokers who had completed a group cessation course	No overall benefit for enhanced support OR 0.99, 95% CI: 0.72, 1.36. There was an interaction effect - men benefited from enhanced support more than women
Roski 2003	System 1: Telephone counselling	System 2: Telephone Counselling + smoker registry and referral system	No benefit for addition of smoker registry and referral system
Katz 2004	Standard care	Standard care vs. intervention to implement clinical practice guidelines (offer of TC and/or NRT	Significant increase in sustained abstinence at 6 months in intervention group OR 3.4, 95% CI: 1.8, 6.3
Hennrikus 2002	Telephone counselling	Group programmes or a choice of TC or group programme	No difference in sustained quit rates
Rodgers 2005	Standard care	Text messaging for tailored support	No significant difference in continuous lapse-free abstinence

NRT refers to nicotine replacement therapy; OR, odds ratio; CI, confidence interval; TC, telephone counselling

Limitations

Trials included in this review were of poor quality of trials with only 6/48 deemed adequate quality by the authors. Randomization methods and allocation concealment were poorly reported and in 24 trials there was no biochemical validation. In addition, point prevalence was used instead of sustained abstinence adding uncertainty to any estimates of effect observed.

Authors' Conclusions

- *Rigorous evaluation of reactive services has been difficult.*
- *Compared to smokers who have only one contact with the quitline, and are either sent self-help materials or receive brief counselling or both, those who receive one or more additional calls have an increased likelihood of quitting.*
- *Proactive telephone counselling helps smokers interested in quitting and there is evidence of a dose response with three or more calls increasing the likelihood of quitting compared to a minimal intervention (providing standard self-help materials).*
- *Larger heterogeneity in studies that recruited participants other than quitline callers; two factors seemed to have influence – intensity of intervention and motivation of participants.*
- *Telephone support as an adjunct to pharmacotherapy detects a small benefit.*
- *Telephone counselling may also have a role in increasing the appropriate use of pharmacotherapy.*
- *Telephone quitlines provide an important route of access to support for smokers and call-back counselling enhances their usefulness.*

3. Interventions for college/ university students

Murphy-Hoefer et al. (2005) was the only systematic review that examined interventions to reduce the prevalence of smoking in college/university students. (5) The following is a summary of the review.

Methods

Studies were considered for the review if they included evaluations of policies or programs designed to decrease tobacco use on college campuses and to provide cessation services for students. Interventions were divided into four categories based on their target population and the type of tobacco use evaluated. The two main categories identified were individual-level interventions (i.e., on-campus cessation programs) and institutional-level interventions (i.e., smoke-free policies). These were further subgrouped according to whether they examined cigarette use or smoke-less tobacco. No pooled analysis was performed due to significant differences between the interventions

Results

Fourteen studies were identified in the review but these were found to be of variable and generally poor quality. Nine studies focused on individual-level interventions and four focused on institutional-level interventions; one encompassed both levels of intervention. Eleven of the studies addressed cigarette smokers, the other three addressed smokeless tobacco. Most of the studies were conducted in the US but two were completed in Europe.

Effects of individual-level interventions

Tobacco Smoking
Seven studies examined individual-level interventions including: educational group and didactic sessions, distribution of self-help materials, individual counselling, computer-assisted cessation education; encouragement of delay of cigarette smoking; scheduled smoking reduction, and the use of nicotine gum. There were no significant differences in quit rates observed between the intervention and control groups.

Smokeless tobacco use
Three studies fell into this category and interventions included: a self-help cessation manual combined with individual counselling, oral examination by a dentist with feedback, behavioural counselling, graphic illustrations of tobacco-related oral lesions, distribution of self-help materials, and telephone follow-up. Studies were generally of poor methodologic quality and the single study that included a comparison group did not report any significant differences in quit rates between the intervention and control groups.

Effect of institutional-level interventions

Tobacco Smoking
Four studies were identified in this category which used smoking restrictions, smoke-free policies, and anti-tobacco messages as their intervention. Study results were reported using a variety of outcomes. One study reported an increased number of quit attempts in the intervention group as compared to the control group whose rates remained constant. A second study found that approximately 30 percent of both men and women surveyed 1 month after the smoking cessation intervention had decreased their cigarette consumption. The third study using the number of cigarette butts collected outside buildings as their outcome measure, reported a significant decrease after the intervention. The final study reported that cigarette price and excise taxes significantly reduced smoking.

Smokeless tobacco use
One study focusing on a policy against the use of smokeless tobacco among athletes did not find any significant differences in smokeless tobacco use following the intervention.

Limitations

As mentioned previously, the majority of studies included in the review were of poor quality due to serious methodological limitations. Studies often lacked comparison groups, randomization, long-term follow up, and/or the power to detect meaningful differences. There was also a lack of valid outcome measures and methods used to ascertain smoking cessation outcomes. Definitions of tobacco use, quit status, and abstinence were similarly variable and unclear, complicating the interpretation of the evidence.

Authors' Conclusions

- *Institutional level interventions aimed at smoking cessation are effective in increasing tobacco use quit rates.*
- *Literature is sparse related to the effectiveness of interventions to promote smoking cessation among college and university students.*

4. Quit and Win Contests

A review by Cochrane assessed the effects of community-based contests such as 'quit and win' style competitions on rates of smoking cessation. (8) The objectives of the analysis also included examining whether the amount and type of incentive alter the rates of smoking cessation and if prizes improve recruitment to community smoking cessation programs. The following is a summary of the review.

Methods

Studies were considered for inclusion if they were RCTs examining population-based quit and win contests at local, national, and international levels compared to a no-contest control group. Controlled trials were also considered if they reported baseline and post-intervention outcomes. Among the outcomes examined were cessation rates, point prevalence, and sustained abstinence for a minimum of 6 months from the start of the intervention. Rates of recruitment and participation in smoking cessation programmes, as well as the public health impact (participation rate x cessation rate) were calculated where possible. Due to the heterogeneity in studies, a meta-analysis was not performed.

Results

Five studies were identified in the review including one RCT, three controlled trials without random allocation, and an observational comparison. Each of these differed in design and the intervention groups also received varying levels of support and access to various smoking cessation strategies (i.e., materials, access to a quitline, online cessation website etc.)

Three controlled studies demonstrated significantly higher quit rates (8% to 20%) for the quit and win group than for the control group at the 12 month assessment mark. In studies where it was possible to calculate the population impact, it was found to be small with fewer than 1 in 500 smokers in communities targeted by quit and win contests quitting as a result of the contest.

Limitations

Only a few studies of variable quality had been published to make up this body of evidence including only one RCT (whose method details were not reported). There were also marked differences between the intervention and control groups examined in the studies in terms of prior exposure to quit and win contests and prior exposure to anti-smoking activities. Furthermore, studies did not always report or quantify baseline differences between the groups. As it is well known that there are high levels of deception in quit and win contests, the populations evaluated may have included never-smokers or ex-smokers biasing findings. In addition, smoking status is usually only biochemically verified in the

winner, which introduces bias into the outcome measurement and verification of baseline smoking. People who join quit and win contests are a self-selected population who may not be representative of the general population. They therefore may also have different relapse rates than those that who do not join contests. This review found that people who joined quit and win contests tended to be female, younger, better educated, in the contemplation or preparation stage of change, and have made more previous quit attempts than those smokers who do not enter contests. All studies were conducted within communities that had current or prior experience of quit and win contests.

Authors' Conclusions

- *Quit and win contests at the local and regional levels appear to deliver quit rates above baseline community rates, although the population impact of the contests seems to be relatively low.*
- *Contests may be subject to levels of deception, which could compromise the validity of the intervention.*
- *International contests may prove to be an effective mechanism, particularly in developing countries, but a lack of well-designed comparative studies precludes any firm conclusions.*

5. Community Interventions

A Cochrane review assessed the effectiveness of community interventions for reducing the prevalence of smoking in adults. (7) Community interventions were defined as "co-ordinated, multidimensional programmes aimed at changing adult smoking behaviour, involving several segments of the community and conducted in a defined geographical area, such as a town, city, county or other administrative district." The following is a summary of the review.

Methods

Studies were included if they were controlled trials randomizing communities or geographical regions, or if they were non-RCTs. The population included was adult smokers (≥18 years of age) and the primary outcome of interest was smoking behaviour, as measured by self-reported smoking status or self-reported cigarette consumption. The review did not exclude studies without biochemical confirmation of self-reported quit status. Intermediate outcomes and process measures were also reported however are not discussed at length in our review of the analysis. Due to the heterogeneity among the studies identified in the literature, a descriptive analysis was provided and meta-analysis was not performed.

Results

The authors identified thirty-seven studies meeting the inclusion criteria, the largest of which were the COMMIT (1995) and CART (2001) trials. In general, the trials were heterogeneous with respect to setting, sample size, intervention purpose, intervention content, education or policy approach, channels through which interventions were delivered, evaluation, and follow up. Approximately 65% of the interventions were aimed at cardiovascular risk factor reduction while nine focused solely on reducing tobacco use. Just under half (46%) of studies compared a single intervention in one community, while the rest included multiple comparison communities or involved multiple intervention and comparison communities. The majority of studies (84%) reported differences in smoking prevalence as their major smoking behavioural outcome and the remainder reported either the changes in the number of cigarettes (or grams of tobacco) smoked per day or quit rates. .

The net decline of smoking prevalence was reported in 31 of the 37 studies and ranged from -1.0% to +3.0% per year. The two most well designed studies showed limited evidence of an effect on prevalence. Cigarette consumption and quit rates were reported in a minority of studies with results reported differently in each, thus no range estimates for these outcomes could be reported.

Because of the heterogeneity in reporting outcomes between the studies, the authors summarized the data based on favourable outcomes, defined as a significant difference in smoking behaviour (for women, men, or both). The investigators reported at least one favourable outcome in 62% of studies but no significant differences in 38% of studies. Two studies that compared more intensive interventions with less intensive interventions did not find significant differences between groups.

Limitations

The studies were generally of poor quality as the trials contained many methodological limitations. For example, 89% of the studies used non-random assignment and only two of the four studies that used random assignment (of matched communities to either the intervention or a comparison group) had adequate power to perform statistical analysis. Bias may have also occurred from errors in statistical analysis using selection of participants, lack of reporting of drop-out characteristics, and a lack of demographically comparable intervention and comparison communities. Comparisons across studies were also complicated by inter-study heterogeneity.

Authors' Conclusions

- *The largest and best designed trials failed to detect an effect of community interventions on smoking prevalence.*
- *Community approaches remain an important part of health promotion activities but the designers of future programmes will need to take into account their limited effect when determining the scale of projects and the resources devoted to them.*

6. Physician Advice to Quit

Cochrane systematically examined the effectiveness of physician advice in promoting smoking cessation. (13) Advice could be brief or part of a more intensive intervention and was defined as *"verbal instructions from the physician with a 'stop smoking' message irrespective of whether or not information was provided about the harmful effects of smoking"*. Additional objectives of the review were to examine whether the level of intensity or the if inclusion of various aids would impact the advice, and to assess the effectiveness of advice on disease-specific and all-cause mortality. The following is a summary of the review.

Methods

Studies selected for the review were those that were randomized and quasi-randomized, and which examined the effect of physician advice on abstinence, assessed with at least six months follow up. The population examined was current smokers; trials that recruited only pregnant women were excluded. The types of trials included were those that compared physician advice to a 'no-advice' or usual care control, or those that compared different intensities of advice. Studies were not included if the physician advice was given as part of a multi-factorial lifestyle counselling intervention. The following definitions were used to describe the intensities of advice:

- Minimal Intervention: provision of advice (with or without a leaflet) during a single consultation lasting less than 20 minutes plus up to one follow-up visit
- Intensive Intervention: intervention involved a greater time commitment than the initial consultation, the use of additional materials other than a leaflet, or more than one follow-up visit.

The primary outcome of the analysis was smoking cessation at six months follow up with a secondary outcome of the effect of physician advice on mortality and morbidity. A meta-analysis was performed using a fixed-effect model and results were expressed using the relative risk of abstinence from smoking.

Results

A total of 41 trials comprising over 31, 000 participants were selected for the review. Of these, 26 were used for pooled analysis of the main comparison between advice and no-advice or usual care control, though it should be noted that the definition of 'advice' varied greatly between trials. In 27 trials, printed materials were given out in addition to verbal advice. These studies were combined with those that included verbal advice only for the pooled analysis. No effect was observed in two studies that examined the additional benefit of providing printed materials to verbal advice alone.

A statistically significant increase in quit rate for brief advice vs. no advice (or usual care), RR=1.66 (95% CI: 1.42, 1.94) was observed in the pooled analysis of 17 trials (Table 4). There was a slightly higher RR of 1.84 (95% CI: 1.60, 2.13) for the subgroup consisting of more intensive interventions, although the authors noted that there is not enough evidence to conclude that there is a significant difference in the effectiveness of physician advice by intensity. In studies that directly compared intensive interventions to those with minimal advice, there was a small but significant benefit for intensive interventions (RR=1.37, 95% CI: 1.20, 1.56). There was an increased effect observed in high risk populations however, this data was derived from five trials and confidence intervals overlapped the results from unselected populations.

The direct effect of additional follow up to a minimal intervention was examined and showed a significant increase in smoking cessation than no follow up (RR=1.52, 95% CI: 1.08, 2.14) although the lower limit of the confidence interval was approaching 1.00. Indirect comparison also suggested an increase in cessation when follow up is provided compared to no follow-up. RR=2.22 (six studies, 95% CI: 1.84, 2.68) vs. RR=1.55 (18 studies, 95% CI: 1.35, 1.79). Studies that used various aids (such as demonstration of expired carbon monoxide levels or pulmonary function tests or self-help manuals) did not show these methods to enhance the effectiveness of physician advice. There was insufficient evidence to determine whether different advice giving styles impact the effectiveness of physician advice. Only one study examined physician advice on subsequent mortality and it showed no significant difference in death rates at 20 years follow-up.

Table 4: Efficacy of physician advice to quit on abstinence from smoking at ≥6 months follow up

Intervention	No. of studies	RR abstinence from smoking at ≥6 months follow up (95% CI)	I^2
Advice vs. Control (subgroups by intensity)	26 trials, N=22,240	1.76 (1.58, 1.95)	39%
1. Minimal intervention*	17 trials, N=13,724	1.66 (1.42, 1.94)	31%
2. Intensive intervention†	11 trials, N=8516	1.84 (1.60, 2.13)	50%
Intensive Advice vs. Minimal Advice	15 trials, N=9775	1.37 (1.20, 1.56)	32%
1. Unselected populations	10 trials, N=6002	1.20 (1.02, 1.43)	0%
2. High risk populations	5 trials, N=3773	1.65 (1.35, 2.03)	21%

RCT refers to randomized controlled trial; I^2 refers to test for heterogeneity

* Defined as provision of advice (with or without a leaflet) during a single consultation lasting less than 20 min and one follow-up visit

† Defined as an intervention which involved a greater time commitment than the initial consultation, the use of additional materials other than a leaflet, or more than one follow-up visit

Limitations

Definitions of advice and follow up times varied considerably among the trials. Randomization and allocation concealment were also not well described in the majority of the trials, creating uncertainty in their methodological quality. Further, only half of the studies reported sustained abstinence and a minority of the trials used biochemical validation of abstinence, which likely resulted in higher quit rates than studies using non-self-report methods. Despite these reservations, exclusion of the poorer quality trials from the pooled analysis did not have an impact on effect size.

Authors' Conclusions

- *Brief simple advice given by physician to their smoking patients increases cessation rates.*
- *Benefit largely depends on the extent to which physicians are prepared to systematically identify their smoking patients and offer them advice as a matter of routine.*
- *Marginal benefits of more intensive interventions, including the use of aids is small and cannot be justified as a routine intervention in unselected smokers. There may be a benefit for high risk smokers.*
- *Strategies should be developed to increase the frequency with which smokers are identified and offered advice and support.*

7. Nursing Interventions

A Cochrane review evaluated the effectiveness of nurse-delivered smoking cessation interventions, each of which included advice that could be used in more intensive interventions. (19) The advice was defined as *"verbal instructions from the nurse with a 'stop smoking' message irrespective of whether or not information was provided about the harmful effects of smoking"*.

Methods

Nursing interventions were classified based on their intensity. Low intensity interventions consisted of a single consultation (with or without a leaflet) lasting 10 minutes or less with a single follow up visit, while high intensity interventions were composed of an initial contact lasting longer than 10 minutes, additional materials and/or strategies other than simple leaflets, and usually more than one follow up. meeting. The population examined in the review was adult smokers and the primary outcome of interest was abstinence from smoking after at least 6 months of follow up. A meta-analysis was performed using a fixed-effect model.

Results

Forty-two studies were identified, of which 31 contributed to the analysis. Five studies were assessed separately as data was not suitable for extraction into a meta-analysis. Studies varied with respect to sample size, setting, patient diagnosis and intervention components. As seen in table 5, there was a statistically significant benefit of nursing interventions on abstinence from smoking at 6 months follow up (RR 1.28; 95% CI: 1.18, 1.38). Indirect comparison showed a greater benefit for high intensity interventions. A higher effect was also seen with interventions for patients with cardiovascular disease, but these results were based on only four trials. There was limited indirect evidence that interventions were more effective for hospital inpatients with cardiovascular disease than for inpatients with other conditions. Interventions among non-hospitalized patients without cardiovascular disease also showed evidence of benefit (RR 1.84; 95% CI: 1.49, 2.28). The five studies not included in the review examined interventions among primary care patients. The authors concluded that "the evidence is not strong for an effect of nurse counselling about smoking cessation when it is provided as part of a health check."

Other results reported by the authors included:

1. Physiological feedback as an adjunct to a nursing intervention failed to detect an effect on smoking cessation rates (two trials)
2. Limited evidence examining effects of other components of an intervention at a single contact
3. Weak evidence that additional telephone support increased cessation
4. No evidence of increased cessation with additional face-to-face sessions

Table 5: Efficacy of nursing interventions on abstinence from smoking at ≥6 months follow up

Comparison	Details	RR abstinence from smoking at ≥6 months follow up (95% CI)	I^2
Advice vs. Control (subgroups by intensity)	31 trials, N=15,205	1.28 (1.18 , 1.38)	54%*
1. High intensity	24 trials, N=11,189	1.28 (1.18, 1.39)	59%
2. Low intensity	7 trials, N=4016	1.27 (0.99, 1.62)	36%
Advice vs. control (subgroups by setting & population)			
1. Intervention as part of multifactorial intervention in patients with cardiovascular disease	4 trials, N= 482	1.39 (1.17, 1.65)	0%
2. Intervention alone in hospitalized smokers with a cardiovascular disease	7 trials, N= 2278	1.29 (1.14, 1.45)	50%
3. Intervention alone in other hospitalized smokers	5 trials, N= 4401	1.04 (0.89, 1.22)	0%
4. Intervention alone in non-hospitalized smokers with a cardiovascular disease	1 trials, N= 255	0.35 (0.20, 0.60)†	___
5. Intervention alone in other non-hospitalized smokers	14 trials, N= 7664	1.84 (1.49, 2.28)	12%

RR refers to relative risk; CI, confidence interval; I^2 refers to test for heterogeneity

* Subsequent analysis excluding three outlying trials lowered the I^2 to 17% and produced an RR of 1.27 (1.18, 1.38)

† Subgroup analysis showed that smokers who had undergone bypass surgery were more likely to quit and were over-represented in the control group

Limitations

Only ~50% of trials included in the review were deemed to be of high quality by the authors. The reasons for the poor quality ratings included the use of convenience samples, lack of reporting of sample size calculations, lack of biochemical validation, and varying definitions of abstinence. Drop out rates also varied considerably across studies. Despite these limitations, a sensitivity of the main analysis encompassing only the high quality studies did not change the main conclusions of the analysis.

Authors' Conclusions

- *Results indicate the potential benefits of smoking cessation advice and/or counselling given by nurses to patients, with reasonable evidence that intervention is effective.*
- *Evidence of an effect is weaker when interventions are brief and provided by nurses whose main role is not health promotion or smoking cessation.*

- *NRT has been shown to improve quit rates when used in conjunction with counselling for behavioural change and should be considered an important adjunct but not a replacement for nursing interventions (Stead 2008)*
- *The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice.*

The authors also stressed that collaboration of many healthcare professionals will likely be required to help individuals achieve smoking cessation. As demonstrated in a 2000 guideline by AHRQ (20), interventions by multiple clinician types are more effective than by a single provider.

8. Interventions for Hospitalized Patients

Cochrane systematically reviewed the effectiveness of interventions for smoking cessation that are initiated in hospitalized patients. (6) The following is a summary of the review.

Methods

Studies considered for the review included randomized or quasi-RCTs and the examined population consisted of hospitalized patients that were either current smokers or recent quitters (trials that focused on patients hospitalized for psychiatric disorders or substance abuse were excluded). Recent quitters were defined as having quit more than one month before hospital admission. The intervention was any type of smoking cessation programme for hospitalized patients that encouraged patients to, or assisted patients in, making a quit attempt, or that aided recent quitters in avoiding relapse. Programmes could include behavioural interventions, pharmacotherapy, and/or advice, with or without follow up after hospital discharge. The control group was comprised of usual care or a group receiving a less intensive intervention than the intervention group. Interventionists could include a variety of professionals including physicians, nurses, smoking cessation counsellors, and other hospital staff. The primary outcome of the study was abstinence from smoking at least 6 months after the start of the intervention. A meta-analysis was conducted using a fixed-effect model.

Results

Thirty-three trials were included in the review with some variation in the patient populations recruited and the level of intensity of the intervention (Table 6). Eighteen studies focused solely on cardiovascular patients, while eleven studies implemented interventions in patients with a wide range of diagnoses.

Table 6: Number of studies subgrouped by intervention intensity

Intervention Intensity	Intensity level definition	# of Studies
Level 1	Single contact in hospital lasting ≤15 minutes, no follow-up support	1
Level 2	≥1 contacts in hospital lasting in total >15 minutes, no f/u support	8
Level 3	Any hospital contact plus follow-up ≤ month	6
Level 4	Any hospital contact plus follow-up >1 month	18

All 33 studies included advice and/or behavioural counselling and in 32 of these a nurse or counsellor provided the advice. The duration of advice/counselling ranged from less than 5 minutes to one hour. Printed or audio materials were also given in most of the trials. The majority of trials also included follow-up support after discharge (25/33 studies), which ranged from 1 week to 6 months after discharge.

The pooled analysis of 17 trials showed that intensive counselling interventions initiated in hospital, and which continued with supportive contacts for at least 1 month after discharge, increased smoking cessation rates (RR=1.40; 95% CI: 1.28, 1.53). There was no significant effect for less intensive interventions. Five trials demonstrated that adding NRT did not produce a statistically significant increase in cessation over what was achieved by intensive counselling alone (RR=1.26; 95% CI: 0.83, 1.91). One study that tested the effect of adding bupropion to intensive counselling also exhibited nonsignificant effect (RR=1.45; 95% CI: 0.82, 2.54).

In the subgroup of studies that examined smokers admitted to hospital for cardiovascular disease, intensive intervention with follow-up support increased the smoking cessation rate to a level similar to that of patients with other admitting diagnoses (RR=1.42; 95% CI: 1.28, 1.57). One trial of intensive intervention, including counselling and pharmacotherapy for smokers admitted with CVD, found significant reductions in all-cause mortality and hospital readmission rates over a 2 year follow up period

Limitations

Recruitment bias may have occurred as only about half of the studies reported methods for randomization and allocation concealment. Biochemical validation was done in the majority of studies (27/33) and most used convenience samples and participation rates were seldom recorders. Sensitivity analyses that excluded poorer quality trials did not differ from the main findings of the analysis.

Authors' Conclusions

- *High intensity interventions that begin during a hospital stay and include ≥1 month of supportive contact after discharge promote smoking cessation among hospitalized patients. These interventions are effective regardless of patient's admitting diagnosis.*
- *Interventions of lower intensity or shorter duration have not been shown to be effective in this setting.*
- *There is insufficient direct evidence to conclude that adding NRT or bupropion to intensive counselling increases cessation rates over what is achieved by counselling alone.*
- *Research is needed to identify effective strategies for implementing this evidence in routine practice in health care systems.*

9. a) Pharmacotherapy: NRT

A review by Cochrane evaluated the effect of NRT compared to placebo in aiding smoking cessation. (12) The authors' objectives were also to examine whether there is a different effect for the various forms of NRT (chewing gum, transdermal patches, nasal spray, inhalers and tablets/lozenges) and to evaluate the effect of combinations of NRT, or NRT compared to other pharmacotherapies.

Methods

Studies were considered if they were randomized or quasi-RCTs. The population examined was current smokers, regardless of their level of nicotine dependence and recruitment setting. The interventions and trials examined included those comparing NRT to placebo or 'no NRT control', trials comparing different NRT doses, and trials comparing NRT combinations to specific NRTs alone. The primary outcome of interest was abstinence from smoking after at least 6 months of follow up. Meta-analyses were performed where appropriate and subgroup analyses were completed for the various forms of NRT. Although some forms of NRT have been licensed for Cut Down to Quit (CDTQ) or harm reduction, these were not examined in this review as they were covered by a separate Cochrane Review (Stead 2007).

Results

The literature search identified 132 trials, 111 of which made up the primary analysis of NRT versus placebo or no NRT control. This analysis produced an RR of 1.58 (95% CI: 1.50, 1.66), demonstrating a benefit of NRT compared to the control group (Table 7). Individually examined NRTs also produced significantly better results than controls, although for certain subgroups there were fewer studies reported, reducing the certainty of effect estimates.

Table 7: Efficacy of NRT on abstinence from smoking at ≥6 months follow up

Comparison	Details	RR abstinence from smoking at ≥6 months follow up (95% CI)	I^2
Any form of NRT vs. placebo/ no NRT control	111 trials, N=43040	1.58 (1.50, 1.66)	24%
Nicotine gum* vs. control	53 trials, N=19090	1.43 (1.33, 1.53)	19%
Nicotine patch vs. control	41 trials, N=18237	1.66 (1.53, 1.81)	20%
Nicotine inhaler vs. control	4 trials, N=976	1.90 (1.36, 2.67)	0%
Oral tablets/lozenges vs. control	6 trials, N=3109	2.00 (1.63, 2.45)	32%
Nicotine nasal spray vs. control	4 trials , N=887	2.02 (1.49, 2.73)	0%

RR refers to relative risk; NRT, nicotine replacement therapy; I^2 refers to test for heterogeneity

*In highly dependent smokers, there was a significant benefit of 4mg gum vs. 2mg, but weaker evidence from higher doses of patch

The authors noted that the effects observed were largely independent of the duration of therapy, intensity of additional support, or setting. They also found a significant increase in cessation for interventions using combinations of NRTs (e.g., nicotine patch with a rapid delivery form of NRT) versus those relying on a single NRT. In studies examining NRTs with other pharmacotherapies, there was evidence of a benefit from the combination of bupropion and a nicotine patch over placebo or patch alone, but not compared to bupropion alone. Results from a pooled analysis with another trial comparing nicotine gum with bupropion to bupropion alone failed to show a significant additional benefit from NRT. Only one study directly compared NRT to another pharmacotherapy and it was found that quit rates with a nicotine patch were lower than those of the bupropion. Finally, three trials directly compared different types of NRT and none detected significant differences.

Adverse Events

There was no quantitative synthesis of adverse events in this report due to variation in reporting, timing, and duration of symptoms among the included trials. The major side effects of NRT are illustrated in Table 8. There has been some concern over the safety of NRT in smokers with cardiac disease however a recent review found no evidence of an increased risk of cardiac events in these patients. (21)

Limitations

The studies included in this review had methodological limitations. In the majority of studies randomization and allocation concealment was poorly described. Abstinence was defined differently across studies and in 24% of studies point prevalence was used rather than sustained abstinence. Four studies were also included based on data from abstracts. Biochemical validation was well done in the trials and was used in all but 14 studies. A sensitivity analysis was performed and exclusion of lower quality trials did not change the main findings.

Table 8: Main side effects reported in analysis of various types of NRT for smoking cessation

Type of NRT	Side effects
Nicotine Gum	Hiccoughs, GI disturbances, jaw pain, orodental problems
Nicotine Patch	Skin sensitivity and irritation*
Inhaler and Nasal Spray	Local irritation at the site of administration
Tablets	Hiccoughs, burning and smarting sensation in the mouth, sore throat, coughing, dry lips and mouth ulcers

NRT refers to nicotine replacement therapy

*Frequent but is usually mild and rarely leads to withdrawal of patch use

Author's Conclusions

The following are the abbreviated conclusions as stated by the authors. For a full list of conclusions please see the original review.

- *All of the commercially available forms of NRT (gum, transdermal patch, nasal spray, inhaler and sublingual tablets/lozenges) can help people who make a quit attempt to increase their chances of successfully stopping smoking. NRT s increase the rate of quitting by 50-70-%, regardless of setting.*
- *The effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the individual.*

9. b) Pharmacotherapy: Antidepressants

A review by Cochrane evaluated the effect of antidepressant medications in aiding long-term smoking cessation. (15) The following is a summary of the review.

Methods

Studies considered for the review were randomized trials comparing antidepressants to placebo or an alternative pharmacotherapy for smoking cessation. Trials comparing different doses, and those that used antidepressants for relapse prevention or cut down to quit were also included. Medications examined included bupropion, doxepin, fluoxetine, imipramine, moclobemide, nortriptyline, paroxetine, sertraline, trytpophan and venlafaxine. The population studied in the review was current smokers or recent quitters in relapse prevention trials. The primary outcome of interest was abstinence from smoking after at least 6 months from baseline. Cigarette consumption and safety outcomes were also examined and meta-analyses were performed where appropriate.

Results

The majority of trials identified from the literature focused buproprion and nortriptyline. Forty trials used bupropion and eight trials were identified for nortriptyline of which three also used bupropion. The literature for other antidepressants was sparse as is described in Table 9.

Table 9: Summary of studies examining Selective Serotonin Reuptake Inhibitors (SSRIs)

Drug	# of studies	Description
Selective Serotonin Reuptake Inhibitors (SSRIs)		
Fluoxetine	4	2 trials tested Fluoxetine vs. placebo 1 trial tested Fluoxetine as an adjunct to nicotine patch; 1 trial as an adjunct to nicotine inhaler
Paroxetine	1	As an adjunct to nicotine patch
Sertraline	1	Versus placebo in conjunction with 6 individual counselling sessions
Citalopram/zimelidine	1	Short-term, examined in heavy drinkers who were not attempting to stop smoking
Other antidepressants		
Doxepin, Imipramine, Tryptophan	0	No long term studies
Moclobemide	1	Long-term placebo-controlled trial
Lazabemide	0	Not being developed
Selegiline	0	Used exclusively as a therapy for Parkinson's disease; NOT as an antidepressant
Venlafaxine	1	1 long-term placebo controlled trial; participants received nicotine patches and 9 brief individual counselling sessions

SSRI refers to selective serotonin reuptake inhibitors

For the Bupropion trials, the majority examined the drug's efficacy compared to placebo (Table 10) and demonstrated that it had a statistically significant effect on smoking abstinence at 6 months (RR 1.75; 95% CI: 1.58, 1.94). There was, however, no evidence of Bupropion providing a benefit when used as an adjunct to NRT (RR 1.31; 95% CI: 0.68, 2.52). Subgroup analyses of follow up duration, clinical setting, and level of behavioural support showed no differences between groups. There authors did not find a statistically significant effect of Bupropion for relapse prevention or for reduction in cigarette consumption. In three trials examining Bupropion compared to varenicline, the latter was found to have a greater effect on smoking abstinence. In a direct comparison of Bupropion versus Nortriptyline, there were no statistically significant differences between the groups, although results favoured Bupropion in each study.

Six studies contributed to the primary analysis of Nortriptyline versus placebo and demonstrated a statistically significant benefit of the drug over the placebo group (RR=2.03; 95% CI: 1.48, 2.78). There was no evidence of benefit found for the use of Nortriptyline as an adjunct to NRT.

Six long term trials of selective serotonin reuptake inhibitors (SSRIs) and other short-term trials failed to demonstrate that this class of antidepressants aids in smoking cessation.

Table 10: Efficacy of antidepressants on abstinence from smoking at ≥6 months follow up

Comparison	Study Size	RR abstinence from smoking at ≥6 months follow up (95% CI)	I^2
Bupropion			
1. Bupropion vs. Placebo (no other pharmacotherapy)	31 trials, N=9940	1.75 (1.58, 1.94)	0%
2. Bupropion + NRT combined therapy vs. NRT alone	4 trials, N=990	1.31 (0.68, 2.52)	67%
3. Bupropion vs. nicotine patch	3 trials, N=657	1.26 (0.73, 2.18)	49%
4. Bupropion vs. varenicline	3 trials, N=1622	0.66 (0.53, 0.82)	0%
5. Bupropion dose response 300 mg/day vs. 150 mg/day	2 trials , N=1833	1.05 (0.90, 1.23)	0%
6. Bupropion vs. Nortriptyline	3 trials, N=417	1.30 (0.93, 1.82)	0%
Nortriptyline			
1. Nortriptyline vs. Placebo (no other pharmacotherapy)	6 trials, N=975	03 (1.48, 2.78)	16%
2. Nortriptyline + NRT combined therapy vs. NRT alone	2 trials, N=318	1.34 (0.90, 2.02)	56%

RR refers to relative risk; CI refers to confidence interval; NRT refers to nicotine replacement therapy; I2 refers to a test for heterogeneity

Adverse events

The main side effects of Bupropion include insomnia, dry mouth, and nausea. Seizures have also been reported with bupropion, however, post-marketing surveillance data has shown that the rates are no higher and possibly lower than 1 in 1,000. There is also concern over the link between antidepressants and reported suicides and death, but a review conducted by the European Agency for the Evaluation of Medicines for Human Use (EMEA 2002) reported that there is insufficient evidence to suggest that any deaths were caused by bupropion.

Nortriptyline has mainly been evaluated in depression studies and its primary side effects are sedation, constipation, urinary retention, and cardiac problems (an overdose of the drug can thus be fatal). In smoking cessation studies the given dose is usually less than that used to treat depression, although due to the low number of studies involving the drug, the safety of the dose sizes used for smoking cessation is still uncertain.

Limitations

Although studies had methodological limitations including poor reporting of randomization and allocation concealment, a sensitivity analysis that excluded lower quality trials did not change the main findings.

Authors' Conclusions

- *Bupropion and nortriptyline aid long-term smoking cessation but selective serotonin reuptake inhibitors do not.*
- *There is insufficient evidence to recommend either bupropion or nortriptyline in preference to NRT or vice versa.*

- *The efficacy of bupropion and nortriptyline appear to be independent of a past history of depression and post cessation depression.*
- *Patient preferences, costs, availability, and side-effect profile will all need to be considered when choosing among medications.*
- *Bupropion and nortriptyline may be helpful in those who fail on NRT.*
- *Recent studies comparing bupropion with varenicline have shown higher quit rates with varenicline.*
- *Adverse events are rarely serious or lead to stopping medication (antidepressants)*

9. c) Pharmacotherapy: Anxiolytic Drugs

A review by Cochrane evaluated the effectiveness of anxiolytic drugs in aiding long term smoking cessation. (10) The following is summary of the review.

Methods

Randomized studies evaluating anxiolytic drugs compared to placebo or an alternative therapeutic control were considered for the review. The medications considered were: buspirone, diazepam, doxepin, meprobamate, ondansetron, metoprolol, oxprenolol, and propanolol. The population examined was 'any smoker' and the primary outcome was abstinence from smoking after at least 6 months from the beginning of treatment. Meta-analyses were performed where applicable using a fixed effects model.

Results

Sparse data exists on anxiolytics for smoking cessation as demonstrated by the low number of trials identified for each medication (Table 11). The authors noted that "*although there are no strongly positive long-term studies, the confidence intervals for the available data do not rule out a possible effect."* In addition, they report that many anxiolytics have significant side effects such as a risk of abuse or dependence and sedation, making them less desirable for smoking cessation.

Table 11: Efficacy of anxiolytics on abstinence from smoking at ≥6 months follow up or cessation rates at 12 months

Comparison	# of trials	RR abstinence from smoking at ≥6 months follow up (95% CI)	Cessation Rate at 12 month follow up
1. Buspirone vs. Placebo	2	0.76 (0.42, 1.37)	
2. Buspirone vs. transdermal nicotine*	1	1.08 (0.70, 1.65)	
3. Diazepam vs. Placebo	1	1.00 (0.56, 1.80)	
4. Meprobamate vs. Placebo	1	Not available; but no beneficial effect	
5. Oxprenolol vs. placebo	1	----------	17% vs. 3%
6. Metoprolol vs. placebo	1	----------	24% vs. 3%†

RR refers to relative risk; CI refers to confidence interval

* Lacked placebo comparison group

† Statistically significant

Limitations

As noted previously there is limited data to evaluate the efficacy of anxiolytics for smoking cessation with only a small number of trials reported.

Author's Conclusions

- *The available evidence neither supports nor rules out an effect of anxiolytics on smoking cessation. In view of this uncertainty and the side effects of the drugs, there is little justification for using them.*

9. d) Pharmacotherapy: Opioid antagonists

A review by Cochrane evaluated the efficacy of opioid antagonists in promoting long-term smoking cessation. (11) The following is a summary of the review.

Methods

RCTs examining the efficacy of opioid antagonists to a placebo or alternative therapeutic control were included in the review. Studies were also included if they compared opioid antagonists as an adjunct to NRT (both Naltrexone and Naloxone were examined in the review). The population of interest was adult smokers and the primary outcome was abstinence from smoking after at least 6 months of follow up. Secondary outcomes included withdrawal, reinforcing or hedonic effects of smoking, mood states and libitum smoking. Meta-analysis was performed using a fixed-effect model.

Results

Few studies meeting the inclusion criteria could be were identified. Four RCTs comprising 582 smokers and all involving the use of Naltrexone on long term abstinence failed to detect an effect of the drug, either as a single pharmacotherapy or as an adjunct to NRT (see Figures 1 and 2).

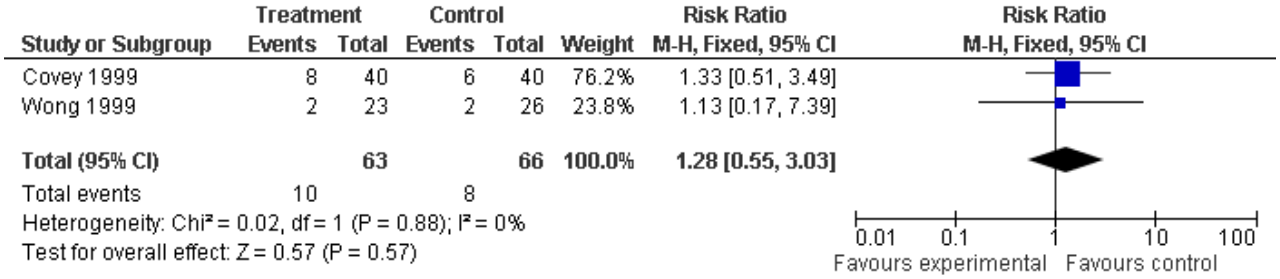

Fig 1: Naltrexone versus placebo for smoking abstinence at longest follow up

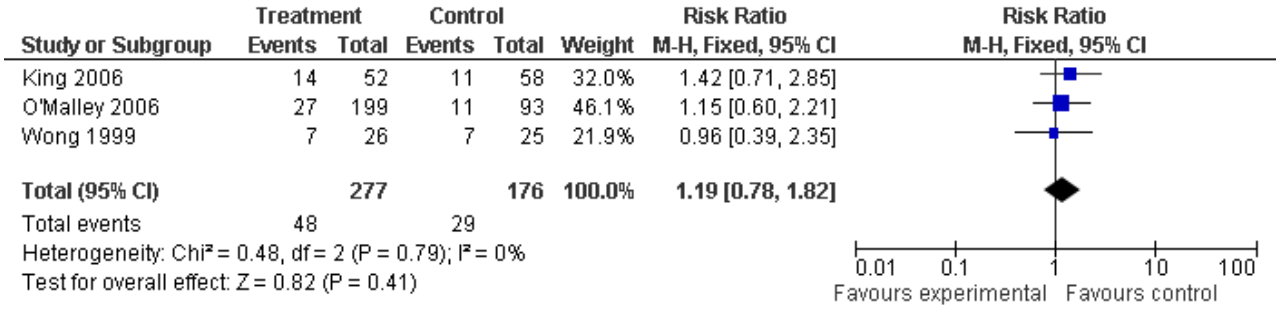

Figure 2: Naltrexone + NRT versus placebo + NRT for smoking abstinence at longest follow up

Secondary outcomes were reported in 14 studies using Naltrexone, five studies using Naloxone, and in two studies using Buprenorphine. The trials reported outcomes differently as identical rating scales were not used. Overall, it was found that Naltrexone alone does not decrease withdrawal symptoms except in a select group of cue reactivity studies. There were mixed findings for both Naltrexone and Naloxone with respect to ad libitum smoking, but a significant increase in rate of ad libitum smoking was observed with Buprenophine (although these studies were conducted in highly specific populations of heroin addicts and opioid- and cocaine-dependent inpatients). Similarly, mixed outcomes were observed for Naltrexone on the reinforcing effects on smoking, while Naloxone had no effect on this outcome.

Limitations

The literature evaluating the effects of opioid antagonists on long-term smoking abstinence is sparse – only four, which all used Naltrexone, were identified. While these trials all confirmed abstinence from smoking with biochemical verification, there was possible allocation bias in two of the studies as they did not report randomization methods.

Authors' Conclusions

- *There is not enough evidence to show the effect of opioid antagonists such as naltrexone for long-term smoking cessation.*
- *Data from larger trials of naltrexone are needed to determine its efficacy for smoking cessation.*

9. e) Pharmacotherapy: Clonidine

A review by Cochrane evaluated the effectiveness of clonidine in helping smokers to quit. (14) The following is a summary of the review.

Methods

Studies considered for the review were randomized trials evaluating clonidine versus placebo for smoking cessation; oral and transdermal clonidine were considered for the treatment arm. The study population included 'any smokers' and the primary outcome of the studies was abstinence from smoking at 12 weeks follow up. A meta-analysis was performed using a fixed effect model.

Results

Six trials met the inclusion criteria for the review, comprising 776 participants. Three of the trials used oral clonidine (0.15 mg/day to 0.45 mg/day) and three used transdermal clonidine (0.1 to 0.3 mg/day). Participants were mainly recruited from community settings (5/6 trials) and the majority of trials described their participants as heavy smokers. Behavioural counselling was offered to all participants in five of the trials.

As shown in Figure 3, clonidine exhibited a statistically significant effect on smoking cessation at 6 months (RR=1.63; 95% CI: 1.22, 2.18), although the trials were of low quality. When studies with short-term follow up were included (15 studies; not shown) the RR was remained significant (RR 1.31; 95% CI: 1.14, 1.51).

The authors reported that clinically significant symptoms of sedation and postural hypotension occurred in a dose-dependent manner in parallel with efficacy making clonidine an unsuitable 'first-line" pharmacotherapy component for smoking cessation. They also highlighted that NRT is preferable for general use and that bupropion is generally better tolerated than clonidine.

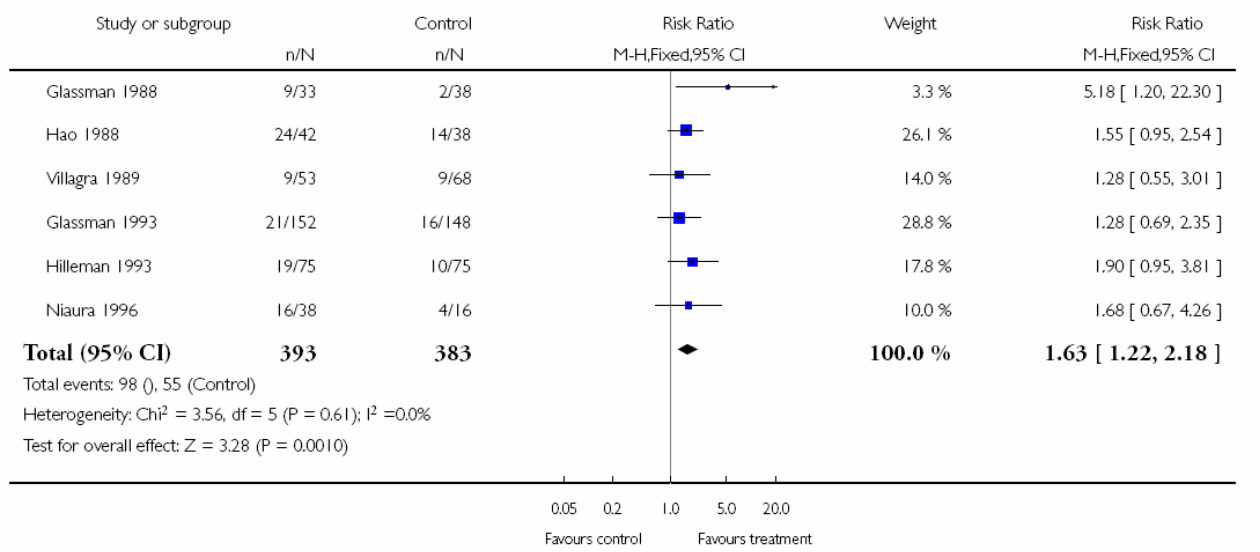

Figure 3: Clonidine compared to placebo for smoking cessation at longest follow up

Limitations

As mentioned previously, the quality of studies included in the review were poor. None reported the details of their randomization procedures or blinding assessment, which has possibly introduced bias into the studies. It was also unclear in any of the trials whether sustained abstinence was required, which likewise may have biased any observed effects. In addition, two of the six studies did not use biochemical verification of abstinence, potentially resulting in a higher estimate of effect.

Authors' Conclusions

- *Clonidine is effective in promoting smoking cessation, however, due to a high incidence of adverse events, such as dry mouth and sedation, clonidine is not a first-line treatment.*
- *Clonidine may be targeted to a subgroup of smokers who would also benefit from its sedative effects. Sedative effects may be desirable if a smoker experiences extreme agitation and anxiety unrelieved by NRT.*
- *Clonidine is unlikely to be used in primary care settings but may play a role in specialist treatment.*

9. f) Pharmacotherapy: Nicotine receptor partial agonists

A review by Cochrane evaluated the efficacy and tolerability of nicotine receptor partial agonists for smoking cessation. (9) The following is a summary of the review.

Methods

Studies were considered for the review if they were RCTs examining the efficacy of a nicotine receptor partial agonist versus placebo for smoking cessation; studies that included comparisons with a NRT or bupropion were also included. The population examined in the studies was adult smokers and the primary outcome of the analysis was abstinence from smoking after at least 6 months from beginning of treatment. Meta-analysis was performed using a fixed-effect model where appropriate.

Results

Ten trials were identified in the literature search, nine on varenicline and one trial on cytisine. A large number of patients were included in the varenicline trials, but they were heterogeneous with respect to their design and purpose (Table 12).

Table 12: Efficacy of varenicline on abstinence from smoking at ≥6 months follow up

Comparison	Details	RR abstinence from smoking (95% CI)	I^2
1. Varenicline vs. Placebo; continuous abstinence at ≥24 weeks	6 trials, N=2582	2.33 (1.95, 2.80)	46%
2. Varenicline vs. Bupropion ; continuous abstinence at 52 weeks	3 trials, N=799	1.52 (1.22, 1.88)	0%
3. Varenicline vs. NRT* (open-label); continuous abstinence at 52 weeks	1 trial, N=757	1.31 (1.01, 1.71)	___
4. Varenicline as Maintenance Therapy; at 52 weeks	1 trial, N=1210	1.18 (1.03, 1.36)	___
5. Varenicline as Maintenance Therapy; at 24 weeks†	1 trial, N=1210	1.42 (1.29, 1.56)	___

RR refers to relative risk; NRT, Nicotine replacement therapy; I^2, test for heterogeneity

* Nicotine patch † End of double-blind phase

As illustrated in Table 12., the pooled analysis of studies examining varenicline versus placebo showed that the drug has a beneficial effect smoking abstinence at 6 months (RR =2.33; 95% CI: 1.95, 2.80). This RR was almost identical observed for continuous abstinence at end-of treatment (RR=2.36, 95% CI: 2.08 to 2.67) and at <24 weeks (2.34, 95% CI: 1.99, 2.75; data not shown). There was also a statistically significant benefit observed for varenicline compared to burproprion, although the authors noted that this data came from only three trials in which buproprion exhibited a poorer performance than what is typically observed. In an open-label trial of varenicline versus NRT, there was a slight benefit of varenicline over the nicotine patch as demonstrated by an RR of 1.31 (95% CI: 1.29, 1.56). When the ability of varenicline to aid in relapse prevention was examined, there was significant effect found at 52 weeks but not at 24 weeks.

The only trial that examined cytisine versus placebo found a significant effect at 6 months (RR 1.91; 95% CI: 1.53, 2.37) and at 2 year (RR 1.61; 95% CI: 1.24, 2.08) follow up. It should be noted, however, that this trial is of poor quality and the results should be interpreted with caution.

The most commonly reported adverse event with varenicline is nausea, however it was generally reported as being mild to moderate, subsiding over time, and it did not impact greatly on discontinuation rates. Post-marketing surveillance has suggested that there may be safety issues due to an increased risk of behaviour change, agitation, depressed mood and suicidal ideation seen in patients taking varenicline. A safety review is currently ongoing. Adverse events reported with cytosine were similar to that of varenicline however only short term data is available.

Limitations

The varenicline trials were generally of high quality with the majority reporting randomization procedures and all trials biochemically verified smoking status. A potential source of bias was that all the trials were industry sponsored. The single cytosine trial was of poor quality since abstinence was self-reported, not biochemically verified, and no details of randomization or allocation methods were given.

Authors' Conclusions

- *Varenicline increased the chances of successful long-term smoking cessation by between two-and three-fold compared with pharmacologically unassisted quit attempts.*
- *More people quit successfully with varencline than with bupropion.*
- *One open-label trial of varenicline vs. NRT demonstrated a modest benefit for varenicline.*
- *The effectiveness of varenicline as an aid to relapse prevention has not been clearly established.*
- *The main adverse event of varenicline was nausea, but mostly and mild to moderate levels and tending to subside over time. Possible links with serious adverse events, including depressed mood, agitation, and suicidal thoughts are currently under review.*
- *There is limited evidence on cytisine and therefore no firm conclusions can be drawn about its effectiveness as an aid to smoking cessation.*

Summary of Results

Based on MAS' summary of the reviews, the following conclusions can be made from this analysis.

1. The evidence suggests that pharmacotherapy, physician advice to quit, nursing interventions, hospital-based interventions, and proactive telephone counselling are effective.
2. There is poor quality data around other population-based smoking cessation strategies including mass media campaigns, community interventions, quit and win contests, access to a quitline, and interventions for university and college campuses, making evaluation of their effectiveness and cost-effectiveness difficult.

Based on pooled summary estimates of effect and safety data (Table 13), the most effective strategies are varenicline, buproprion, nicotine replacement therapies, followed by physician advice to quit and nursing interventions in non-hospitalized smokers without cardiovascular disease.

Table 13: Summary of pooled estimates from meta-analyses

Intervention	RR abstinence from smoking at ≥6 months follow up (95% CI)	Comment
NRT – any type	1.58 (1.50-1.66)	111 trials
Antidepressants		
Buproprion	1.75 (1.58-1.94)	31 trials
Nortriptyline	2.03 (1.48, 2.78)	6 trials
Nicotine partial antagonists - varenicline	2.33 (1.95, 2.80)	6 trials
Clonidine	1.63 (1.22, 2.18)	6 trials; significant adverse events
Opioid antagonists	No evidence of effect	
Anxiolytics	No evidence of effect	
Physician advice to quit – brief advice	1.66 (1.42, 1.92)	17 trials
Nursing interventions		
Intensive interventions	1.28 (1.18, 1.38)	24 trials
In non-hospitalized smokers without CVD	1.84 (1.49, 2.28)	14 trials
Telephone counselling		
Trials providing access to a helpline	Not estimable	2 trials
Additional proactive calls (people calling quitlines)	1.36 (1.23, 1.50)	8 trials
Proactive counselling interventions	1.29 (1.19, 1.40)	29 trials
Hospital-based interventions		
Intensive with at least 1 month follow up	1.40 (1.28, 1.53)	17 trials

RCT refers to randomized controlled trial; CVD refers to cardiovascular disease; NRT refers to nicotine replacement therapy

Economic Analysis

DISCLAIMER: The Medical Advisory Secretariat uses a standardized costing method for its economic analyses of interventions. The main cost categories and the associated methods from the province's perspective are as follows:

Hospital: Ontario Case Costing Initiative cost data are used for in-hospital stay, emergency visit and day procedure costs for the designated International Classification of Diseases (ICD) diagnosis codes and Canadian Classification of Health Interventions procedure codes. Adjustments may be required to reflect accuracy in estimated costs of the diagnoses and procedures under consideration. Due to the difficulties of estimating indirect costs in hospitals associated with a particular diagnosis or procedure, the secretariat normally defaults to considering direct treatment costs only.

Nonhospital: These include physician services costs obtained from the Ontario Schedule of Benefits, laboratory fees from the Ontario Schedule of Laboratory Fees, drug costs from the Ontario Drug Benefit Formulary, and device costs from the perspective of local health care institutions whenever possible or its manufacturer.

Discounting: For cost-effectiveness analyses, a discount rate of 5% is applied as recommended by economic guidelines.

Downstream costs: All numbers reported are based on assumptions on population trends (i.e. incidence, prevalence and mortality rates), time horizon, resource utilization, patient compliance, healthcare patterns, market trends (i.e. rates of intervention uptake or trends in current programs in place in the Province), and estimates on funding and prices. These may or may not be realized by the system or individual institutions and are often based on evidence from the medical literature, standard listing references and educated hypotheses from expert panels. In cases where a deviation from this standard is used, an explanation is offered as to the reasons, the assumptions, and the revised approach. The economic analysis represents ***an estimate only***, based on the assumptions and costing methods that have been explicitly stated above. These estimates will change if different assumptions and costing methods are applied to the analysis.

Study Question

The objective of this project was to provide the Ministry of Health Promotion (MHP) with a summary of recent reviews on clinical and economic outcomes of population-based smoking cessation strategies.

Economic Literature Review

Given the time-sensitive nature of the request, a scan of the economic literature was conducted and recent published reviews were appraised and reported. A systematic search was not performed. A literature search was instead conducted of relevant databases (see Appendix 1) for recently published article reviews, HTAs, and Cochrane Reviews of the following smoking cessation strategies:

1. Mass Media Interventions
2. Telephone Counselling
3. Post-Secondary Smoking Cessation Programs (colleges/universities)
4. Community-wide Stop-smoking Contests (Quit and Win)
5. Community Interventions
6. Physician Advice to Quit
7. Nursing Interventions
8. Hospital-based Interventions
9. Pharmacotherapy

The Cochrane Reviews did not address cost-effectiveness (CE) and no recent HTAs addressing either effectiveness or cost-effectiveness of cessation interventions could be identified. Published article reviews of economic analyses were then reviewed. Kahende (22) et al. published a review in 2009 that compiled economic evaluations such as cost analyses, cost-effectiveness analyses (CEA), cost-utility analyses (CUA), and cost-benefit analyses (CBA) from 1983 to 2006. (22) This comprehensive economic literature review included 42 economic papers (all costs reported in 2005 American dollars, USD).

Results

Kahende et al. identified two studies examining the CE of mass media campaigns. One evaluated the costs and outcomes of a Scottish public anti-smoking campaign that included three components: a) advertising in television, outdoor posters and press; b) a telephone quitline for cessation support; and c) an advice booklet. The cost per life year saved (C/LYS) ranged from $671 to 1,330. The second study estimated the CE of a 4 year mass media campaign added to a school curriculum for adolescents (ages 10 to 16). The authors concluded that the cost per smoker averted was $939 and the C/LYS was $867.

Three CEAs evaluating community-based interventions were identified. The first, known as the 'Breathe Easy' project, was a 4-year community based research project to help women (ages 18 to 64) quit smoking to be with an estimated C/LYS of a $2,087. A second study compared the CE of a pharmacist-directed program and estimated the C/LYS to be $844 to $1,662. The third study evaluated a separate pharmacy based smoking cessation program using data from two pharmacies in Northern Ireland. The program included a written contract between the pharmacist and patient with a defined stop date and a series of counselling sessions over a 6 month period. The authors reported the C/LYS to be $393 to $701 in men and $363 to $1,541 in women and concluded that these results compare favourably with other disease prevention medical interventions.

Two studies evaluating the CE of quitlines were identified, the first of which examined the American Cancer Society's telephone counselling service. They reported that the cost of each case of maintained cessation attributed to the telephone service was $1,475 yearly. Another studied evaluated the CE of a public quitline service in Sweden. The study included 1,131 callers enrolled in the program and the authors concluded that the program was cost-effective with a C/LYS ranging from $343 to $443.

The review identified several studies that examined economic evaluations of pharmacotherapy. Most of these were short-term examinations of abstinence from 2 weeks to up to one year. The CE ratio ranged from $1,400 to $14,000. The authors of the individual studies concluded that pharmacological therapies could be cost-effective as compared with other medical interventions.

Four studies focusing on counselling were also identified, including group therapy for smoking cessation. The first evaluated the CE of the 1996 Smoking Cessation Clinical Practice Guidelines plus or minus nicotine patch/gum. They reported a cost per quality-adjusted life year (QALY) range of $1,491 to $5,818. The second study analyzed the CE of physician counselling during routine office visits. The authors reported a C/LYS of $1,325 to $3,869 for both women and men. The authors concluded that counselling was as cost-effective as other preventive medical practices. A third study evaluated the CE of a smoking cessation program delivered by hospital nurses to smokers admitted for myocardial infarction. The authors found that the C/LYS was $306 per year. The fourth study evaluated the CE of a smoking cessation and relapse prevention program for hospitalized adult smokers. The interventions included a 20-minute bedside counselling session, a 12 minute video, self-help materials, and a number of follow-up calls. The C/LYS ranged from $2,229 to $9,811, which the authors concluded was cost-effective.

Table 14 summarizes the incremental cost-effectiveness ratios (ICER) associated with each strategy reported in the review.

Conclusion

Kahende et al. reported that most strategies were cost-effective. Although this is true when based on the ICER ranges reported in the review, given the limited clinical effectiveness data reported earlier, caution should be advised when interpreting the results of the economic literature review.

Table 14. Results of the Kahende 2009 Review

Intervention	Outcome	ICER
Mass Media Campaigns (2005 USD)		
Anti-smoking campaign – mass media advertising: TV, posters and press; smokeline; booklet	Cost per quitter Cost per life year saved	$341-678 $671-1,330
4 year mass media campaign in adolescents – added to school based tobacco education curriculum – grades 5-7; continued to grades 8-10	Cost per smoker averted Cost per life year saved	$939 $867
Community-Based Interventions (2005 USD)		
4 year, multifaceted research project: the Breathe Easy project in women 18-64 years of age	Cost per life year saved	$2,087
Program in a community pharmacy practice – written contract with a defined 'stop date'; series of counselling meetings over 6 months	Cost per life year saved	Men: $393-701 Women: $362-1,541
Program in a community pharmacy vs. self-directed quit attempt	Cost per additional patient to quit Cost per life year saved	$277 $844-1,662
Program in a community pharmacy vs. nicotine patch	Cost per additional patient to quit Cost per life year saved	$1,097 $844-1,662
Program in a community pharmacy vs. nicotine gum	Cost per additional patient to quit Cost per life year saved	$2,109 $844-1,662
Program in a community pharmacy vs. Bupropion	Cost per additional patient to quit Cost per life year saved	$1,348 $844-1,662
Quitlines (2005 USD)		
American Cancer Society's telephone counselling service	Cost per case of maintained cessation per year	$1,475
Swedish quitline service	Cost per quitter Cost per life year saved	$1,161-1,500 $343-443
Pharmacotherapy (2005 USD)		
NRT plus counselling	Cost per life year saved	$9,231
NRT plus physician advice vs. physician advice	Cost per additional lifetime quitter Cost per quality adjusted life year	$9,392 Men: $5,624-14,018 Women: $6,347-8,945
Nicotine gum	Cost per life year saved	$4,031

Intervention	Outcome	ICER
Nicotine patch	Cost per life year saved	$2,152
Nicotine spray	Cost per life year saved	$4,992
Nicotine inhaler	Cost per life year saved	$4,660
Bupropion	Cost per life year saved	$1,438
Free gum + physician counselling	Cost per quitter	$1,673
9 dollar gum + physician counselling	Cost per quitter	$418
30 dollar gum + physician counselling	Cost per quitter	$617
NRT patch plus physician counselling	Cost per life year saved	$791 (<35 ys)
NRT patch plus physician counselling	Cost per life year saved	$686 (35-44 ys)
NRT patch plus physician counselling	Cost per life year saved	$859 (45-54 ys)
NRT patch plus physician counselling	Cost per life year saved	$1,561 (55-65 ys)
NRT patch plus physician counselling	Cost per life year saved	Men: $2,301-3,778 Women: $3,894-$5,625
NRT plus counselling vs. counselling	Cost per life year saved	$2,540-7,621
Bupropion plus counselling vs. counselling	Cost per life year saved	$1,580-4,743
NRT/Bupropion plus counselling vs. counselling	Cost per life year saved	$2,085-6,256
Counselling and Group Therapy (2005 USD)		
Smoking Cessation Clinical Practice Guidelines +- patch/gum	Cost per quitter Cost per QALY	$4,841 $1,491-5,818
Physician counselling to quit during routine office visits	Cost per life year saved	Men: $1,325-1,857 Women: $2,264-3,869
Smoking cessation program delivered by nurses in the hospital to smokers admitted for MI	Cost per life year saved	$306
Smoking cessation and smoking relapse prevention program for hospitalized adult smokers – 20 min bedside session; 12 min video; self-help materials; FU calls	Cost per quitter Cost per life year saved	$4,873 $2,229-9,811

ICER = Incremental Cost-Effectiveness Ratio

Conclusions

1. The evidence suggests that pharmacotherapy, physician advice to quit, nursing interventions, hospital-based interventions and proactive telephone counselling are effective and cost-effective in the short-term.
2. There is poor quality data around other population-based smoking cessation strategies including mass media campaigns, community interventions, quit and win contests, access to a quitline, and interventions for university and college campuses making evaluation of their effectiveness and cost-effectiveness difficult.
3. Based on pooled summary estimates of effect and safety data, the most effective strategies are varenicline, buproprion, nicotine replacement therapies, followed by physician advice to quit and nursing interventions in non-hospitalized smokers without cardiovascular disease.

Appendix: Literature Search Strategies

Smoking Cessation – Economics – Search Strategy*

Search date: July 22, 2009
Databases searched: OVID MEDLINE, EMBASE, CRD/INAHTA

Database: Ovid MEDLINE(R) <1950 to July Week 2 2009>
Search Strategy:
1 exp "Tobacco Use Cessation"/ec [Economics] (582)
2 exp "costs and cost analysis"/ (144428)
3 exp "Tobacco Use Cessation"/ (13913)
4 3 and 2 (480)
5 4 or 1 (762)
6 limit 5 to (english language and yr="1998 -Current") (611)
7 limit 6 to "review" (97)

Database: EMBASE <1980 to 2009 Week 29>
Search Strategy:
1 *smoking cessation/ (7179)
2 exp "cost effectiveness analysis"/ (59331)
3 (economic* or cost-effective*).ti,ab. (109136)
4 1 and (2 or 3) (405)
5 limit 4 to (english language and yr="1998 -Current") (282)
6 limit 5 to "review" (62)

*A very quick scan as per request to pick up major review articles

References

(1) Rehm J, Baliunas D, Brochu S, Fischer B, Gnam W, Patra Jet al. The costs of substance abuse in Canada 2002: highlights [Internet]. Ottawa, ON: CCSA. 2006 Mar 1. [cited: 2010 Oct 14]. 12 p. Available from: http://www.ccsa.ca/2006%20CCSA%20Documents/ccsa-011332-2006.pdf

(2) The Ontario Tobacco Research Unit. The burden of tobacco use in Ontario [Internet]. [Toronto, ON]: OTRI. 2006 Jun. [cited: 2010 Jan 14]. 2 p. Available from: http://www.otru.org/pdf/updates/update_june2006.pdf

(3) Canadian Tobacco Use Monitoring Suvey (CTUMS). Canadian tobacco use monitoring survey (CTUMS) 2007 [Internet]. [updated 2008 Dec 8; cited 2010 Jan 14]. Available from: http://www.statcan.gc.ca/cgi-bin/imdb/p2SV.pl?Function=getSurvey&SurvId=4440 &SurvVer=1&InstaId=16040&InstaVer=16&SDDS=4440&lang=en&db=imdb&adm=8&dis=2

(4) Ministry of Health Promotion. Creaing a smoke-free Ontario [Internet]. [updated 2009 Jan 20; cited 2009 Aug 8]. Available from: http://www.mhp.gov.on.ca/english/health/smoke_free/accomplishments.asp

(5) Murphy-Hoefer R, Griffith R, Pederson L, Crossett L, Iyer S, Hiller M. A review of interventions to reduce tobacco use in colleges and universities. Am J Prev Med 2005; 28(2):188-200.

(6) Rigotti NA, Munafo MR, Stead LF. Smoking cessation interventions for hospitalized smokers: a systematic review. Arch Intern Med 2008; 168(18):1950-60.

(7) Secker-Walker R, Gnich W, Platt S, Lancaster T. Community interventions for reducing smoking among adults. Cochrane Database Syst Rev 2002; Issue 1. Art. No.: CD001745. DOI: 10.1002/14651858.CD001745.

(8) Cahill K, Perera R. Quit and win contests for smoking cessation. Cochrane Database Syst Rev 2008; Issue 1. Art. No.: CD004986. DOI: 10.1002/14651858.CD004986.pub3.

(9) Cahill K, Stead LF, Lancaster T. Nicotine receptor partial agonists for smoking cessation. Cochrane Database Syst Rev 2008; Issue 1. Art. No.: CD006103. DOI: 10.1002/14651858.CD006103.pub3.

(10) Hughes JR, Stead LF, Lancaster T. Anxiolytics for smoking cessation. Cochrane Database Syst Rev 2000; Issue 2. Art. No.: CD002849. DOI: 10.1002/14651858.CD002849.

(11) David S, Lancaster T, Stead LF, Evins AE. Opioid antagonists for smoking cessation. Cochrane Database Syst Rev 2006; Issue 2. Art. No.: CD003086. DOI: 10.1002/14651858.CD003086.pub2.

(12) Stead LF, Perera R, Bullen C, Mant D, Lancaster T. Nicotine replacement therapy for smoking cessation. Cochrane Database Syst Rev 2008; Issue 4. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub3.

(13) Stead LF, Bergson G, Lancaster T. Physician advice for smoking cessation. Cochrane Database Syst Rev 2008; Issue 1. Art. No.: CD000165. DOI: 10.1002/14651858.CD000165.pub3.

(14) Gourlay SG, Stead LF, Benowitz NL. Clonidine for smoking cessation. Cochrane Database Syst Rev 2004; Issue 2. Art. No.: CD000058. DOI: 10.1002/14651858.CD000058.pub2.

(15) Hughes JR, Stead LF, Lancaster T. Antidepressants for smoking cessation. Cochrane Database Syst Rev 2007; Issue 3. Art. No.: CD000031. DOI: 10.1002/14651858.CD000031.pub3.

(16) Bala M, Strzeszynski L, Cahill K. Mass media interventions for smoking cessation in adults. Cochrane Database Syst Rev 2008; Issue 1. Art. No.: CD004704. DOI: 10.1002/14651858.CD004704.pub2.

(17) Stead LF, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database Syst Rev 2006; Issue 1. Art. No.: CD002850. DOI: 10.1002/14651858.CD002850.pub2.

(18) Rice VH, Stead LF. Nursing interventions for smoking cessation. Cochrane Database Syst Rev 2008; Issue 4. Art. No.: CD001188. DOI: 10.1002/14651858.CD001188.pub3.

(19) Rice VH, Stead L. Nursing intervention and smoking cessation: meta-analysis update. Heart Lung 2006; 35(3):147-63.

(20) Fiore MC, Bailey WC, and Cohen SJ. Treating tobacco use and dependence. A clinical practice guideline. Rockville, MD: 2000.

(21) Joseph A, FU S. Pharmacotherapy for smoking in patients with cardiovascular disease. Prog Cardiovasc Dis 2003; 45:429-41.

(22) Kahende JW, Loomis BR, Adhikari B, Marshall L. A review of economic evaluations of tobacco control programs. Int J Environ Res Public Health 2009; 6(1):51-68.