

A review of interventions for smoking cessation

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Abstract

Background

Diverse interventions for cessation of smoking, pharmacological and otherwise, have been studied, with less attention being paid to unassisted cessation. Tobacco and pharmaceutical industries, too, have interests in cessation, assisted or otherwise.

Aims

To review evidence for interventions for smoking cessation.

Methods

The search included the Cochrane Tobacco Addiction Group, PubMed and Google Scholar.

Results

Most ex-smokers have quit without professional input. Motivational interviewing (MI), nicotine replacement therapy (NRT), varenicline, bupropion and nortriptyline show effectiveness. Clonidine is effective but has serious side effects. Naltrexone is ineffective. Brief interventions by doctors, structured interventions by nurses, MI and other individual therapies, mobile phone-based interventions, and telephone counselling are effective. E-cigarettes have opposing evidence of effectiveness and harm.

Conclusions

Pharmacological methods seem to focus on managing withdrawal, and hold little promise in managing or preventing relapses, except varenicline. Despite heavy emphasis placed on NRT, nortriptyline seems to be safer, cheaper and equally effective. Brief advice given by doctors is as effective as NRT.

Which non-pharmacological method work best with regards to relapse prevention is yet to be determined. Psychiatrists may use MI or personalised psychoeducation with or without nortriptyline, NRT, bupropion or varenicline. Clonidine is reserved as a second line intervention for inpatients. NRT may also be useful for temporary withdrawal of tobacco use for heavy smokers who are unwilling to quit. E-cigarettes are not to be recommended. Further research on unassisted cessation, safer interventions such as simple advice, and the role of tobacco and pharmaceutical industries is needed. New treatment guidance, better informed by evidence, is warranted.

Key words: smoking cessation, unassisted quitting, nicotine replacement therapy, motivational interviewing, nortriptyline

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Introduction

Smoking remains the single most preventable cause of death and disease (1). It accounts for 5.4 million deaths worldwide and 20,000 deaths in Sri Lanka every year (1,2). Many interventions are available to assist smokers to quit, but most quit attempts are unaided by professionals (3-5).

All health workers are expected to provide smokers help to quit. This includes physicians, nurses and other health workers. However, a special emphasis is placed on psychiatrists as they are considered to be experts in dealing with addictions. Many options are at the disposal of the psychiatrist to choose from in helping his or her patients to quit smoking. They are either pharmacological or non-pharmacological. Pharmacological options include nicotine replacement, naltrexone, varenicline, bupropion and other interventions. Motivation enhance-

ment therapy and other individual psychological therapies and brief interventions are some of the non-pharmacological therapies. The use of a combination of pharmacological and non-pharmacological options seems to be popular (6).

Cognitive behaviour therapy is widely known to be effective in addiction psychiatry (7). However, there have been very little research published on CBT for smoking cessation. This is probably due to the availability of less intensive treatment strategies, such as telephone counselling, that may incorporate CBT techniques. One study has shown that group based CBT is effective in assisting smoking cessation (8).

Cigarette smoking can be viewed as a “communicated disease” according to former Director-General of the WHO Dr. Gro Harlem Brundtland, who called it a disease “communicated through marketing” (9). The WHO

intends to reduce the initiation, as well as promote to the cessation of use, in its work in prevention of tobacco related disease and death (9,10). Both these objectives are in direct confrontation with the objectives of the tobacco industry (9). In this context, it is interesting to note that the tobacco industry has done extensive research on smoking cessation from 1980 or before (11), provided funding to researchers in tobacco control, and is reported to have manipulated, suppressed and used research to the advantage of the industry (9). These observations raise questions as to whether the tobacco industry might have had an influence on the current smoking cessation literature, including treatment guidelines. For example the observation that smoking cessation leads to weight gain may tempt the smoker to postpone quitting, which is favoured by tobacco industry. A Cochrane review on interventions to reduce post-cessation weight gain found no evidence of effectiveness with pharmacological interventions, while observing behavioural interventions showed better potential (12).

Chapman and MacKenzie note that up to 75% of ex-smokers have quit without professional help or medication, despite rising emphasis on the disease model of smoking and the requirement of professional advice including pharmacological input to manage the disease (4). They also show researchers have paid disproportionate level of attention (91.3% of studies examined) to assisted smoking cessation, and many such studies are funded by pharmaceutical industry involved with manufacture of pharmacological products available for smoking cessation (4).

Unassisted smoking cessation has been researched only sparingly. However the evidence suggests this to be a potentially highly effective way of quitting smoking. A total of 26 population-based prevalence studies of unassisted quitting have been identified, which presented data collected from 1986 through 2010, in 9 countries (5). Unassisted quit attempts ranged from a high of 95.3% in a study in Christchurch, New Zealand, between 1998 and 1999, to a low of 40.6% in a national Australian study conducted between 2008 and 2009. In 24 of the 26 studies reviewed, a majority of quit attempts were unassisted (5).

Current scientific discourse, including guidelines popular among psychiatrists, highly recommend assisted quitting, especially using pharmacological methods. Researchers are doing increasingly sophisticated research, such as genomic analysis to guide choice of pharmacological agents for smoking cessation (13). NRT, which is only modestly more effective than placebo, receives a prominent place in treatment guidelines (14). A BMJ editorial emphasises that NRT may not be as effective in real world as indicated in clinical trials. It also observes that naturalistic studies show that smokers who stop without pharmacological interventions have better long term outcome (15). It is interesting to

examine the possibility whether this heavy emphasis on assisted quitting, especially on pharmacological interventions, is due to the influence of the tobacco and pharmaceutical industries. In this context, this search was planned to review the available evidence for interventions for smoking cessation.

Methods

A search was carried out on the Cochrane Tobacco Addiction Group (TAG), PubMed and Google Scholar databases. TAG is a resource centre established to prepare and maintain systematic reviews of interventions relevant to tobacco control. The relevant articles from the TAG list of 60 reviews categorised under 'Interventions to help smokers and other tobacco users to quit' were searched. The keywords used for PubMed were 'smoking cessation' and 'outpatient' with a filter set to select review articles only. The same keywords were used in Google Scholar, limiting the search to the first 100 relevant recent reviews. The search was limited to publications in English language. Relevant articles cited within the selected articles were also retrieved and assessed. A narrative approach was used to synthesise evidence.

Results

Nicotine replacement therapy (NRT)

Clear evidence exists to support the effectiveness of NRT in smokers who do or do not use other psychoactive substances (16-18). The latest Cochrane review (2012) concludes that NRT in all available forms, skin patch, gum, nasal spray, inhaler, lozenge and sublingual tablet, increase the success rate of highly dependent (ten to 15 cigarettes or more per day) smokers who are motivated (16). Success rates of being abstinent at six to twelve months from the quit attempt without any professional help are 5% or less. When these quit attempts are supported by NRT, the rate is estimated to rise by 2 to 3% for the same time period. The authors have calculated a number needed to treat to benefit (NNTB) in this review, which is estimated to be 56 (16).

All forms of nicotine delivery have similar effects and the duration of treatment to be effective seems to be eight weeks (16). Gradual withdrawal of NRT does not seem to have an additional advantage, compared to abrupt cessation (16). NRT in the form of skin patches worn during waking hours only have the same effect as wearing it for all 24 hours (16). NRT in the form of gum, fixed dose or as needed, show similar efficacy (16). Smokers who have failed with 2mg gum or who are deemed to have very high level of dependence, may have an added benefit with 4mg gum (16). More than one form of NRT can be combined, and skin patch with gum used as needed seemed to be most effective (16). Starting NRT before the quit date renders no added advantage except in the case of skin patches (16).

The efficacy of NRT is higher if the smoker has been motivated by other inputs before use, but adding intensive support to NRT does not increase the efficacy (16). The efficacy of NRT is comparable to bupropion (16). It is also noted that repeat use of NRT after failure produces only a small benefit (16). NRT is not found to increase cardiovascular events in vulnerable smokers (16).

Concerns have been raised regarding efficacy and safety of NRT in people who try to stop multiple drug use and about any negative effects on recovery from dependence on other drugs. Two systematic reviews, one of them a Cochrane review (2016), found that NRT is effective in those who have undergone or are undergoing management of alcohol or other drug use disorder as either in- or outpatients, without having any negative effect on recovery from other drug or alcohol use disorders (17,18).

Antidepressants

Bupropion

According to a 2014 Cochrane review, high quality evidence is available to indicate that bupropion is effective in aiding smoking cessation (19). Bupropion increases success rates by 1.5 to 1.8 times compared to other single interventions, which is comparable to various behavioural interventions and NRT (19). It is effective in diverse populations including smokers with or without a past history of depressive disorder, but is more effective than nortriptyline in smokers with past or current depressive disorder (19). However bupropion is not shown to mediate any added benefit as an adjunct therapy to NRT (19). Although the recommended dose of bupropion is 300 mg per day, there is some evidence to suggest that 150 mg per day is as effective (19). Seizures, suicides and deaths have been reported, but evidence is still not conclusive that they are due to bupropion (19).

Nortriptyline

Moderate quality evidence is available to prove that nortriptyline is effective in aiding smokers to stop smoking according to a Cochrane review (19). Nortriptyline, similar to bupropion, does not add any benefit to NRT (19). There are no direct comparisons with NRT or varenicline, but available evidence on comparison with bupropion suggests that they both are effective at similar levels (19). It is notable that, unlike bupropion, no serious side effects have been reported with nortriptyline, while also noting that the sample size of that study was small (19).

Nicotine receptor partial agonists

Varenicline

High quality evidence is available to prove that varenicline is effective in aiding smokers to stop smoking compared to treatment without pharma-

cological agents according to a Cochrane review (20). Some evidence exists to indicate that varenicline may be more effective than bupropion and NRT (20). Varenicline given at sub-standard doses (less than 2 mg per day) still proved to be as effective as NRT and bupropion, and caused fewer side effects (20). Serious adverse effects have been noted such as change of behaviour including agitation, depressed mood and suicidality (20). The Cochrane review casts some doubt on the causal relationship of these adverse effects, but the FDA has issued a warning on serious neuropsychiatric adverse effects (20). The cardiovascular adverse effect profile of varenicline is not yet clear (20).

Cytisine

Some evidence is available to suggest that cytisine is modestly effective in aiding smokers to stop smoking (20).

Other pharmacological and physical methods

Naltrexone

Clear evidence is available that naltrexone is not useful in aiding smokers to quit smoking, nor does it add any benefit to the effects of NRT if combined in treatment (21).

Anxiolytics

According to another Cochrane review, diazepam, meprobamate, metoprolol, oxprenolol and busprione do not show any significant impact on aiding smokers to stop smoking, although these findings had wide confidence intervals (22).

Clonidine

Clonidine appears to be effective in aiding smokers to quit, comparable with NRT and bupropion, however sedation and postural hypotension prevents its wide usage, as effective doses tend to worsen adverse effects (23). These adverse effects are clinically significant and occur in a dose-dependent manner in parallel with efficacy (23).

Acupuncture

Low quality evidence indicates that acupuncture and related therapies do not seem to be effective in aiding smokers to stop smoking, according to a Cochrane review (24).

Simple interventions by doctors and nurses

Physicians advice

Brief advice from doctors is shown to be effective, with a calculated NNTB of 35-50, which is comparable to NNTB of NRT(25). Following up with the initial advice seems to have an additional benefit (25). In addition to

brief advice, if support for smoking cessation is offered, the frequency of quit attempts is significantly increased (26).

Nursing interventions

A recent systematic review of 19 studies designed and executed by nurses found out that nursing interventions for hospitalised patients are effective. Most of the studies reviewed have examine structured interventions characterised by educational messages using multiple formats, counselling, and, especially, follow up (27). A much older Cochrane review suggests that structured, non-brief and consistent interventions by nurses aimed at cessation of smoking is modestly effective (28).

Psychological interventions

Motivational interviewing

Evidence exists to show that motivational interviewing is effective in promoting smoking cessation, especially if delivered by general practitioners in short sessions lasting less than 20 minutes. No clear evidence is found on the appropriate number of follow up sessions (29).

Individual counselling

A Cochrane review examined various studies that incorporated individual face to face talking therapy of various durations by varied providers incorporating CBT or psychoeducation or self-help or motivational components. The meta-analysis showed that individual counselling was effective in helping people to quit (30). It has been shown, at least among people with smoking and other substance use, intensive CBT per se may not be more effective than other interventions, especially combinations (18). Another Cochrane review found that hypnotherapy is not effective as a smoking cessation intervention (31).

Phone based interventions

Mobile phone based interventions

Text messages, motivational as well as educative, sent via mobile phone has been shown to assist smoking cessation (32).

Telephone counselling

Telephone counselling (quit lines) aimed at smoking cessation comprising three or more calls has been found to be more effective than providing self-help materials or brief advice or pharmacological interventions only (33).

E-cigarettes

The latest Cochrane review (January 2016) found that there were only two RCTs covering e-cigarettes that met inclusion criteria. A meta analysis based on these two studies indicated that e-cigarettes are significantly

more effective than placebo e-cigarettes in aiding smokers to stop smoking (34). Another systematic review (of 38 studies) which incorporated a meta analysis (of 20 studies), published at same time (January 2016) found that e cigarettes tend to lower the quitting rate (35). The authors of the latter study warned against the use of e-cigarettes as a therapeutic intervention in smoking cessation unless proven to be effective (35).

Abrupt quit

When studies comparing abrupt and gradual quitting are examined, a review found no method is superior to the other (36). The studies included looked at interventions with or without NRT or individual psychological input.

Relapse prevention

Interventions helpful in prevention of relapses are recognition and management of high risk situations, and varenicline administered for longer periods of time (37). No other pharmacological method is successful in relapse prevention, but more research is needed to study the effectiveness of other psychological interventions (37).

Policy and legislative interventions

Although policy and legislative interventions are not typically reviewed in treatment intervention reviews in smoking cessation, one interesting and well-conducted recent 'systematic review of reviews' revealed that such interventions are effective (38). Price hikes, graphic pictorial warnings and clean indoor laws are some of the interventions studied by the papers they have reviewed (38).

Discussion

A majority of smokers who quit and subsequently stay abstinent for long periods of time do so on their own without professional input. This review assessed the evidence for effectiveness of the options available for doctors to offer to patients seeking help to quit their smoking.

Motivational interviewing, NRT, varenicline, bupropion, nortriptyline, counselling input from doctors and nurses appear to show effectiveness over placebo in getting more people to quit and stay abstinent for six to twelve months. Naltrexone is not useful in aiding smoking cessation.

Nicotine replacement to treat withdrawal symptoms is comparable to benzodiazepine prescription in alcohol withdrawal, and similarly dosing needs to be judged according to the severity of dependence. Skin patches are the slow-release form of NRT, while others such as gum act as treatments with rapid onset of action. For

obvious reasons, a combination of the slow release form and a rapid acting form would be beneficial, and is proven to be so. Typically smokers receive a dose of nicotine less than through their smoking habit, and therefore it is bound to be less hazardous than smoking.

NRT is prominently featured in many treatment guidelines for management of smoking and information sources for smokers wanting to quit (14,39,40). It has been added to the model list of essential medicines compiled by the World Health Organization (41). However it is interesting to note that NRT has an NNTB comparable to that of brief advice from physician. Another notable finding is that many smoking cessation studies are funded by producers of pharmacological agents which are promoted to help cessation (4).

Further, treatment guidelines advise to give NRT along with advice or guidance or counselling. Although evidence points out that adding intensive support to NRT does not increase its efficacy (16), no clear evidence exists to prove NRT without a counselling input is effective. However, one RCT ($n=2,591$) found that free NRT without a counselling input has been demonstrated to be ineffective (3).

The concern regarding prominence given versus actual real-world effectiveness of NRT equally applies to varenicline and bupropion. However, varenicline appears to have the highest efficacy out of these three pharmacological methods, although it carries a certain risk of serious neuropsychiatric adverse effects at standard doses. Lower doses of varenicline appear to be safer and as effective as NRT or bupropion. Risk of cardiac events with varenicline is not yet determined. Nortriptyline appears to be effective with a more favourable adverse effects profile in aiding smokers to quit despite the concern about toxicity in overdose.

Varenicline is an $\alpha_4\beta_2$ nicotinic receptor partial agonist, thus it is expected to moderate the low dopamine levels during nicotine withdrawal, and also to moderate the high dopamine levels during smoking (42). Bupropion is thought to inhibit noradrenaline and dopamine reuptake in effecting an antidepressant effect, which is thought to be important in aiding smoking cessation (43). Nortriptyline is a tricyclic antidepressant (44) and is the cheapest option (45), although unavailable in Sri Lanka.

Clonidine, though effective, has serious side effects, therefore it is not considered as a first line therapy. Other pharmacological agents, such as naltrexone and anxiolytics, need further research to, if ever, be accepted as effective smoking cessation interventions. According to available data, acupuncture is not an effective option that can be offered to smokers to help quitting.

Brief interventions by doctors and structured nursing interventions appear effective in aiding people to stop

smoking. These interventions are extremely unlikely to have adverse effects and they are low-cost practical acceptable interventions. The effectiveness of simple one-time advice from doctors on quitting can be further enhanced by follow up advice or checking and offering quitting support.

Individual face-to-face talking therapy of various styles, including motivational interviewing, is found to be effective in aiding smokers to stop. Although again safe, they take up a considerable amount of time and effort as well as expertise to deliver.

Innovative interventions using mobile phones, mostly through text messages, and counselling delivered via telephone with follow up calls are found to be effective in helping smokers to quit. Texting services have a high potential, as they are, once set up, extremely economical to deliver with a wide reach.

E-cigarettes have created a considerable controversy as the renowned Cochrane review system tends to favour e-cigarettes as effective quitting aids, while another systematic review and meta analysis examining a much larger number of studies directly challenge the Cochrane review recommendations. The Cochrane review admits to the controversy in its text (34). Serious concerns regarding e-cigarettes and other smokeless tobacco products have been expressed. Firstly, the associated risks of causing serious health harms such as malignancies, oral conditions, cardiac disease and strokes are undetermined at the moment (46). Secondly, they appear to be a gateway to cigarette smoking especially for the youth (46).

Abrupt versus gradual withdrawal does not seem to make a significant difference in the end. None of the pharmacological methods seem to hold any promise in treating or preventing relapses, except, perhaps, varenicline. More data is needed to determine which non-pharmacological method, if any, would work in relapse prevention.

Conclusions

Despite heavy emphasis placed on NRT, bupropion and varenicline, nortriptyline seems to be a safer, cheaper and an effective pharmacological intervention to aid tobacco cessation. Brief advice given by doctors may be as effective as NRT, however patients may expect a more sophisticated intervention from a psychiatrist. Motivational interview or personalised psycho-education with or without nortriptyline (or another tricyclic) may be used by psychiatrists. NRT, bupropion and varenicline are also possible contenders for the pharmacological option. Clonidine may be reserved for the rare patient with severe dependence willing to have a short inpatient stay for the detoxification. NRT may also be useful for temporary withdrawal of tobacco use for heavy smokers unwilling to quit but who require short term abstinence, such as for air-travel or short hospital stays.

Novel and more evidence informed treatment guidance for smoking cessation, including guidance on the role of clinicians on unassisted quitting, targeting medical undergraduates, general physicians, psychologists, public health specialists, psychiatrists and other clinicians is a pertinent need.

NRT, theoretically a simple detoxification agent, modestly more effective than placebo, receiving wide recognition as the mainstay treatment in smoking cessation arouses doubt about the process of its rise to this position. The undue prominence attracted by assisted quitting, while non-assisted quitting seems to be equally if not more prevalent and effective, feed into the same suspicion. The controversial role played by tobacco and pharmaceutical industries needs to be further explored. The recommendation of e-cigarettes as a therapeutic quitting agent exemplifies this need.

Further research regarding effective smoking cessation interventions is acutely needed. Firstly, as certain potentially effective interventions such as simple advice, as well as 'atypical interventions' such as clean indoor laws, have not been well studied. Secondly, extensive research in assisted cessation reminds us that the role of unassisted cessations is neglected. Thirdly, the role of tobacco and pharmaceutical industries in smoking cessation requires more extensive and rigorous investigation.

Conflicts of interest

None declared

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