

20 YEARS OF THE COCHRANE TOBACCO ADDICTION GROUP: PAST PRESENT AND FUTURE

*Nicola Lindson-Hawley PhD¹; Laura Heath MBBS ¹; Jamie Hartmann-Boyce MA¹

¹Cochrane Tobacco Addiction Group, Nuffield Department of Primary Care Health Sciences,
University of Oxford, Radcliffe Observatory Quarter, Woodstock Road, Oxford, OX2 6GG

Correspondence to: nicola.lindson-hawley@phc.ox.ac.uk

*Corresponding author

Abstract

Cochrane is a global organisation committed to carrying out high standard systematic reviews and meta-analyses to inform healthcare and those associated with it, from patients to providers. **The** Cochrane Tobacco Addiction Group (TAG) has been reviewing the evidence for interventions to treat and prevent tobacco addiction for 20 years. During this time the group has published over 70 reviews in the area, which have had substantial impacts on healthcare guidance and treatment provision. This has coincided with a reduction in smoking prevalence in the UK. One of the groups' key objectives is to move with the times and it does this by updating historical reviews with the most up to date evidence, but also by commissioning or accepting requests for new reviews in novel areas, such as electronic cigarettes and plain packaging. This review paper highlights the previous important work that the group has done and its impacts, what is happening within the group more currently, and also describes where Cochrane TAG wish to go in the future and the work being done to solidify aims. Part of this is a prioritisation project being carried out to mark the 20th anniversary of the group, which is using stakeholder engagement to inform an action plan to inform the outputs and aid dissemination to ensure Cochrane TAG's work is relevant and maximises impact for the next 20 years.

Implication

This review provides an overview of the work of the Cochrane Tobacco Addiction Group. Readers will gain an insight into the origins of the group, its impact on evidence based medicine relating to tobacco addiction and the goals of the group moving forward. This supports the group's aim to encourage knowledge of Cochrane's work within the field, and thereby the wider use of and contribution to high quality systematic reviews and meta-analyses of the literature to improve policy and clinical practice.

Introduction

Tobacco is the leading cause of preventable death worldwide and the health impacts associated with use are substantial and diverse. Tobacco accounts for 80% of deaths due to lung cancer; 80% of deaths due to bronchitis and emphysema; and 14% of deaths related to ischaemic heart disease. It also causes over 25% of cancers including bladder, lip, throat, mouth, kidney, pancreas and cervix ⁵. On average, smokers die 10 years before their non-smoking counterparts ⁵. In order to reduce such morbidity and mortality, the establishment of effective evidence-based policies has become a major global health priority. Due to the vast amount of material available on the subject, however, establishing which interventions are most effective is often difficult for policy makers.

It has been estimated that the total cost to the UK of tobacco smoking is £13.9 billion per **year**¹¹ and therefore returns on investments into tobacco control are likely to be great. The UK All Party Parliamentary Group on Smoking and Health recently estimated that increasing the UK government expenditure by £100 million per year would likely see a 1100% return on the investment over five years ¹¹. Providing a reliable, evidence based framework will enable investments to be used wisely and potential health and economic returns maximised (See Box 1. for a very brief history of evidence based medicine).

Since 1996 the University of Oxford's Cochrane Tobacco Addiction Group (TAG) has systematically collated and reviewed studies relating to tobacco interventions. These evidence-based reviews have been used to inform changes in policy and clinical practice guidelines for tobacco use globally. The aim of this paper is to give a background to the origins of the group, highlight some of the important work carried out to date and its impact, review some recent findings, and look to the future by identifying some upcoming projects.

Cochrane Tobacco Addiction Group (TAG)

Cochrane TAG currently have a suite of approximately 70 completed reviews on the topic of tobacco use treatment and prevention, with many including meta-analyses of primary study data. They also manage some ‘orphan’ reviews- systematic reviews on topics which do not fit within any other subject specific Cochrane review groups - on subjects from eLearning in healthcare to food allergies. The group have a team made up of hundreds of external review authors who they assist to carry out reviews; however, TAG’s editors also author a number of reviews themselves. (See Box 2. for a brief history of Cochrane and Box 3. for a history of Cochrane TAG)

The aims of Cochrane TAG’s research are:

- to inform tobacco control policy internationally;
- to inform research in tobacco control, and to help ensure new research is focussed on important unanswered questions;
- to contribute to reducing tobacco use.

Though a solid evidence base is crucial in any area, in tobacco the need for unbiased evidence is particularly strong. Competing interests, including those of the tobacco industry, can heavily influence publications. By systematically collecting evidence, assessing it for methodological issues, and implementing thorough analyses, TAG has amassed unbiased and comprehensive bodies of evidence for life-saving interventions. These reviews are regularly updated, which makes them dynamic and able to account for developments in the literature.

Smoking prevalence has fallen in the UK since TAG was formed (See Figure 1), though the direct relationship between guidelines, practice, and smoking prevalence cannot be quantified. When the group began, the prevalence of smoking in the adult population of the UK was 28% ¹⁶. In 1998, the UK government published its white paper ‘Smoking Kills’¹⁷ which set out a range of interventions for reducing smoking prevalence in the UK and included a substantial investment in smoking cessation services. This white paper was based on UK national guidelines, which drew on evidence from Cochrane TAG’s reviews. In the subsequent years, the prevalence of adult smoking in the UK has fallen to below 20% and there are over two million fewer adult smokers in the UK ¹⁶. There is substantial evidence of the impact of TAG’s research on the policies that have been implemented during this period, and the below highlights the use of three Cochrane reviews in guidelines and practice shaping documents.

Case studies- findings and impact

The following case studies of Cochrane TAG reviews give an idea of the work carried out by the group. All three were written by members of the group’s editorial base: one of NRT; one of physician advice; and one of telephone counselling, all for smoking cessation.

Nicotine replacement therapy (first published 1996)

Since the first version of the Cochrane review of NRT, this review has been updated regularly (see Figure 2). The first version included 72 studies; it now contains 150. This review investigates different forms, delivery methods and settings, schedules, and dosages of NRT in a range of subgroups, and shows definitively that all commercially available forms of NRT

help people to quit smoking relative to placebo or no NRT control (RR 1.60, 95% CI 1.53 to 1.68) ¹⁸.

This review provided evidence for a 2008 proposal for the inclusion of NRT in the World Health Organization (WHO) list of essential medicines, which described the review as “the largest database on the effectiveness of NRT.” ¹⁹. This proposal was approved in May 2009. The recommendation was said to be supported by Cochrane TAG’s “high-quality evidence of effectiveness” ²⁰. WHO predicted that the inclusion of NRT on the list of essential medicines would advance guideline development and improve access to NRT in developing countries ²⁰.

Beyond international use, the NRT review has been cited in three key national UK guidelines in recent years, which continue to shape practice. The evidence review ²¹ underpinning NICE guidance on Brief Interventions and Referral for Smoking Cessation recommends the use of NRT based on the Cochrane review. Guidelines published from the US ²² and Australia ²³ also cite the review, using it as consistent evidence for use of NRT as a medication to aid smoking cessation and using it to support the specific recommendation that heavily dependent smokers use higher doses of oral NRT. In the case of US guidelines²², the review was cited alongside an extensive meta-analysis conducted by guideline developers.

In addition to its use in guidelines, the NRT review has also recently been used to inform point of care material ²⁴ and patient information sources ²⁵ in the UK.

Physician advice (first published 1996)

This review has been updated eight times since first publication, currently includes 41 trials, and demonstrates that brief clinical advice is associated with a significant increase in the rate

of quitting (RR 1.66, 95% CI 1.42 to 1.94), in comparison to no advice or usual care. The association was found to be dose responsive - stronger with more intensive advice (see Figure 3) ⁶.

Many physicians were initially reluctant to advise patients not to smoke, as the efficacy of the approach was doubted and there were concerns it would affect the doctor-patient relationship. However, the Cochrane TAG review of physician advice for smoking cessation has been used in numerous guidelines as definitive evidence for the efficacy of this approach, and has shaped practice accordingly.

Australian guidelines ²³ use the review to support the assertion that all health professionals should systematically identify smokers and offer them treatment advice at every opportunity, using the summary statistic from the review in support of brief motivational advice. In a table listing barriers to health professionals providing smoking cessation services, one of the seven barriers listed is the belief, “I am not effective.” The Cochrane review is cited as evidence that this is not the case. US guidelines ²² and the NICE Rapid Review of Brief Interventions and Referral for Smoking Cessation cite the review as evidence that brief advice from a physician is effective ²¹, and is consistent with the meta-analysis conducted by US guideline developers on the topic²².

Telephone counselling (first published 2000)

This review has been updated six times since first publication and contains 65 trials. Higher quit rates were found in participants randomized to multiple sessions of proactive counselling (RR 1.38, 95% CI 1.28 to 1.49), and telephone counselling not initiated by calls to helplines was also shown to increase quit rates (RR 1.29, 95% CI 1.20 to 1.38) ²⁶.

Quitlines are widely available throughout North America, Europe, and Asia, and are a major area of public health investment in many countries. TAG's review of telephone counselling has informed the current and continued funding of these quitlines. The review has also informed specific aspects of telephone counselling methods.

Australian guidelines²³ cite the review in support of the use of proactive calls and provide summary statistics to illustrate the overall efficacy of telephone counselling. In the evidence review for NICE's guidelines on The Impact of Quitlines on Smoking Cessation²⁷, they report that Cochrane TAG's review "provided a key source of information" for the guidelines and it is cited as strong evidence for both proactive phone counselling and additional sessions of phone counselling. In addition, US Guidelines²² use the review as the sole source of evidence that quitlines significantly increase abstinence rates.

These examples are by no means comprehensive, and represents only three of a body of around 70 reviews. These reviews have been used to shape policy and practice not only in the UK, the US and Australia, but also in countries as diverse as Canada, Finland, Paraguay, Portugal, and Uruguay. In addition, the UK National Centre for Smoking Cessation and Training use a variety of Cochrane TAG's reviews to inform the training that they provide for smoking cessation practitioners.

New evidence

The above provides information on TAG's long term achievements and contributions; however with the ever changing landscape of tobacco addiction treatment, and the evolving

treatment needs of those who continue to smoke, the landscape of research into tobacco control is still changing. It is vital that TAG's reviews accommodate this to ensure that they remain useful and valid.

A prime example of this was the recent publication (2014) of a new review for the group, looking at the effects of electronic cigarettes (EC) on smoking reduction and cessation²⁸. The review was the first attempt made to systematically review the literature on this topic. In doing so it highlighted the small amount of high quality evidence evaluating EC (with only two randomised controlled trials meeting the criteria for inclusion), despite an enormous increase in their use and in interest and discussion on the subject in recent years. The review found that, "Participants using an EC were more likely to have abstained from smoking for at least six months compared with participants using placebo EC (RR 2.29, 95% CI 1.05 to 4.96; placebo 4% versus EC 9%; 2 studies;)"²⁸. However, this needs to be considered alongside the fact that the authors rated the quality of the evidence as 'Low' by GRADE standards²⁹, due to imprecision as a result of the small number of trials. This means that further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate in the future. Despite this, the review garnered a great deal of publicity worldwide, following a press release and a news briefing by the authors at the Science Media Centre in London, UK. The review is very likely to influence future healthcare guidance, as it is currently one of the only sources of systematic, high quality evidence on a high profile subject. The next update of the review is planned for 2016.

Similarly the group recently aided the update of a review of legislative smoking bans on health outcomes,³⁰ which also attracted a lot of media attention - again largely because it is the result of the most thorough attempt to systematically review the topic to date. Unlike

many of the reviews published by Cochrane TAG, all of the evidence presented in this review is from observational studies. This makes it very difficult to account for potential confounding, but even taking this into consideration it was concluded that there was moderately strong evidence to conclude that smoking bans lead to a reduction in heart disease and deaths from smoking-related illnesses, and that the greatest drop in hospital admissions for heart disease was in populations of non-smokers. This information is particularly important in the context of public health policy decisions and is a key illustration of how Cochrane reviews can be useful in this regard, and not just in informing clinical and personal treatment decisions.

Moving forward

Cochrane TAG intends to move forward following three distinct workstreams, outlined below. These directions have been chosen to maintain the group's momentum and to ensure the group continues to contribute to developments in the field.

Adapting updates of reviews by responding to changes in the use of existing treatments

One of the strengths of the Cochrane method is the development and publication of review protocols. This ensures transparency and therefore minimises bias. However, it is also important to adapt to developments in the field. For example NRT was originally used in singular form, however it is now common to use it in combination (e.g. a patch in combination with a short acting form, such as gum). It was important that the review accommodated this change in order to inform clinicians and the public about the safety and effectiveness of using NRT in this way. As long as any changes to methods remain

transparent and are explained in the update this is essential to keeping Cochrane reviews relevant.

Developing new protocols and publishing new reviews to further widen the Cochrane evidence base

Although TAG can identify necessary topics for review and either carry these out themselves or contact potential external author teams, existing or potential authors are encouraged to liaise with Cochrane TAG about any ideas they may have for new reviews they would like to carry out (See Box 4. for more information on how to get involved). The group have an editorial base that can then discuss the proposal and ensure that it is relevant to the group, that it is not covered by an existing review, and that the author team have the necessary expertise to carry out the review, with support. This takes into account that Cochrane themselves offer training in their methods, and so it is not imperative that proposed authors have carried out a Cochrane Review before. Through working with external author teams Cochrane TAG plan to publish a number of new reviews in the next year, including investigations of institutional smoking bans, tobacco packaging design, and treatment in primary care and psychiatric settings.

Speaking to our stakeholders

Until now, TAG's review portfolio has been shaped by researchers. However, this year, as part of our 20th anniversary celebrations, we proposed to speak to our stakeholders through a priority setting exercise, involving public and stakeholder dialogue. A two-part survey on questions that still need to be answered in tobacco control was distributed to policy makers, healthcare providers, smokers, former smokers, guideline developers, researchers and research funders, February to May 2016. This was followed by a one-day workshop in June,

during which the review portfolio was reviewed in light of the previously identified questions and future priorities set - for new reviews, updating existing reviews, and considering ways in which the TAG portfolio could better meet the needs of a broader user group. Broadening input will ensure reviews meet a wide range of needs, are relevant to current trends in smoking, and therefore create the highest possible impact, whilst guarding against research wastage. The James Lind Alliance advocate such an approach and we drew on their key principles to pioneer this inclusive methodological approach to priority setting. The results of this exercise will be written up for peer reviewed publication and presented, and the group will begin work on the priorities identified.

Conclusion

In conclusion, Cochrane TAG's work investigates and summarises the literature base for interventions aiming to prevent or treat tobacco addiction, focusing on the areas that will be most relevant to users. In doing so reviews to date have had a wide and deep impact across guideline development and treatment services. The group's aims going forward are to ensure that this continues and to adapt to emerging trends. As time goes on this will become a less straightforward task, and therefore it makes sense for TAG to harness the ideas of the people they wish to help and ask them what is important to them. With finite resources it is important to remain focused on relevant questions to drive the field forward and assist in reducing and treating tobacco use.

Funding

The Cochrane Tobacco Addiction Group is funded by the National Institute for Health Research (NIHR). The Cochrane TAG twentieth anniversary priority setting (CTAG taps)

project is funded by the NIHR School for Primary Care Research. The views expressed are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

Declaration of Interests

NLH is co-investigator on a trial testing nicotine patch preloading, funded by the NIHR, Health Technology Assessment programme. The pharmacotherapy used in the intervention arm of this trial were provided free of charge by GlaxoSmithKline plc. None of the trial investigators are directly employed by GlaxoSmithKline plc and GlaxoSmithKline plc had no involvement in the design, conduct or analysis of the trial. JHB & LH have no declarations of interest.

Acknowledgements

We gratefully acknowledge Cochrane Tobacco Addiction Group (TAG) funding from the NIHR, as well as all employees and contributors to the work of Cochrane TAG past and present.

Box 1. History of Evidence Based Medicine

‘Evidence based medicine’ was a phrase first used by Gordon Guyatt, an internal medicine resident at McManus University in the early 1990s ¹. He had benefitted from mentoring by Dr David Sackett, a clinician with public health training, who was responsible for the implementation of the first clinical epidemiology course at McManus University in 1967, and was the first to describe ‘critical appraisal’ ³.

Others too had sought to increase the scientific rigour of clinical decision making. Dr Alvan Feinstein used his mathematical background to collect data about patients from the Rheumatic Fever Hospital in New York. He knew that there were biases and error in interpreting murmurs at the bedside and used his epidemiological data to transform the care these patients received, ultimately resulting in the closure of the hospital due to lack of patients ⁷. He was also the first to use the phrase ‘clinical epidemiology’ ^{9 12 14} in three papers published in the *Annals of Internal Medicine*.

Suzanne and Robert Fletcher were also substantial contributors to the formation of this new movement. Both U.S. doctors, they had recognised the gap between research and clinical decision making, and after qualifying in clinical medicine and public health established a medical epidemiology course at McGill University Medical School and published *Clinical Epidemiology: The Essentials* in 1982. Prior to this, the accepted way to practise medicine was predominantly expert opinion and there was little translation of epidemiology or trial data into clinical decision making.

Box 2. What is Cochrane?

The formation of Cochrane can be attributed to three individuals: Iain Chalmers, Tom Chalmers and Murray Enkin. The organisation was named after Archie Cochrane, who was the first individual to promote the use of Randomised Controlled Trials (RCTs) to reduce study biases. As a prisoner of war in World War 2, he used randomisation on his fellow prisoners to study whether yeast extract affected the development of deficiency disease ². Later, he was known for the Rhodda Fach study ⁴, which looked at the role of Tuberculosis versus dust in the development of progressive pulmonary fibrosis. Tom Chalmers recognised the importance of Archie Cochrane’s work and was the first to describe a hierarchy of evidence, culminating in RCTs, systematic reviews and meta-analyses and to highlight the risks of publication bias ⁸. Tom Chalmers and Iain Chalmers collaborated with obstetrician Murray Enkin to pool all the current study data relating to the care of pregnant women, which ultimately led to the publication of ‘*Effective Care in Pregnancy and Childbirth*’ ¹⁰ and the formation of the Cochrane Collaboration in 1993. Early results from the group were instrumental in revolutionising care in the perinatal period, including the final cessation of the use of diethylstilbestrol and role of administering steroids to mothers of preterm infants.

Today, Cochrane (as it is now more simply called) is a global not for profit organisation dedicated to reviewing the available healthcare literature, with a strong emphasis on detecting potential biases. It does this using systematic review and meta-analyses methods, which are detailed in the Cochrane Handbook. The aim of this is to provide a high quality evidence base to inform healthcare decisions. It is made up of over 50 topic specific review groups who review the literature in particular topic areas.

Box 3. History of the Cochrane Tobacco Addiction Group (TAG)

Cochrane is an organisation made up of many Review Groups (see Box 2.). Cochrane TAG was one of the first Cochrane Review Groups to be established. It was founded by Chris Silagy, Tim Lancaster and Godfrey Fowler, who were all general practitioners working in the General Practice Research Group (GPRG), within the Department of Public Health, University of Oxford. GPRG had a research focus on smoking cessation, and had conducted one of the first trials of the use of nicotine patches for smoking cessation in a primary care setting.

Through his work in Oxford, Chris Silagy had met Iain Chalmers, who was working on establishing the Cochrane Collaboration, and Chris became involved in helping to drive the concept forward. The first review produced by TAG was a systematic review of nicotine replacement therapy (NRT) for smoking cessation. This was a prototype Cochrane review, used to test the methodologies and software of the collaboration. This review, many times updated, remains in the Cochrane Library 24 years later. Work to go on and review other smoking cessation interventions was initially funded by the Imperial Cancer Research Fund (ICRF) - now known as Cancer Research UK (CRUK). In 1995, the decision was made to establish a Cochrane Review Group focussing on interventions to prevent uptake of smoking and to help people to quit. From 1996, this work was funded by the NHS Research and Development stream; and later by the National Institute for Health Research, who still fund the group today.

Following the NRT review, the next reviews TAG managed focused on physician advice ⁶, acupuncture and hypnotherapy to help people quit smoking ¹³, followed by a review covering anxiolytic and antidepressant pharmacotherapies ¹⁵.

Box 4. How you can get involved

- **Comment on our reviews – register with our group to review our outputs before they come out (email Cochrane.tobacco@phc.ox.ac.uk)**
- **Help identify areas where we should be conducting reviews – as an author if you like! (email Cochrane.tobacco@phc.ox.ac.uk)**
- **Help identify reports of randomized controlled trials through Cochrane Crowd (<http://crowd.cochrane.org/faq.html>)**
- **Participate in other tasks (e.g. translation) through Cochrane Task Exchange (<http://taskexchange.cochrane.org/>)**
- **If you're a patient, carer or member of the public, consider joining the Cochrane Consumer Network (Consumers.Cochrane.org). This is based in over 79 countries and provides training and support to help consumers identify research priorities, work alongside researchers to produce reviews, and check the readability and help to write plain language summaries.**

Figure 1: Graph of smoking prevalence in the UK alongside key Cochrane Tobacco Addiction Group review updates

Figure 2: Illustration of the key characteristics and updates of the Cochrane Tobacco Addiction Group nicotine replacement therapy review

Figure 3: A forest plot of the effect of physician advice smoking cessation advice versus control (subgroups by intensity of advice); outcome: smoking cessation at longest follow up

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