National Institute for Health and Care Excellence

Guideline version (Final)

Smoking cessation interventions and services

Systematic review appendices

NICE guideline NG92

Appendices

March 2018

November 2021: NICE guideline NG92 (March 2018) has been updated and replaced by NG209. The recommendations labelled [2018] or [2018, amended 2021] in the updated guideline were based on these evidence reviews.
See www.nice.org.uk/guidance/NG209 for all the current recommendations and evidence reviews.

FINAL

These evidence reviews were developed by Public Health Internal Guideline Development team

Disclaimer

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or service users. The recommendations in this guideline are not mandatory and the guideline does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or their carer or guardian.

Local commissioners and/or providers have a responsibility to enable the guideline to be applied when individual health professionals and their patients or service users wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with compliance with those duties.

NICE guidelines cover health and care in England. Decisions on how they apply in other UK countries are made by ministers in the Welsh Government, Scottish Government, and Northern Ireland Executive. All NICE guidance is subject to regular review and may be updated or withdrawn.

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Appendix A: Methodology

A.1 Original methodology

A.1.1 Stepped approach to evidence identification

The stepped approach includes the use of all elements of a comprehensive search strategy, but structures the approach as a set of 'steps' which inform decisions as to whether subsequent elements of the searching (and reviewing) are necessary to meet the needs of the committee considering update or development of recommendations. A detailed search strategy is provided in Appendix B:

Step 1	**Search CDSR**[1] to identify Cochrane Systematic Reviews
Step 2	**Identifying primary studies** to supplement the Cochrane Reviews with more up to date information
Step 3	Identifying evidence from **grey literature** applicable to the UK
Step 4	**Named interventions** search for specific programmes, initiatives or services identified from sifting the results from steps 1-3.
Step 5	Additional searches to identify **cost effectiveness and economics** literature
Pause	Gap analysis to prioritise next searching activity. The next steps could include some or all of the following:
Step 6	Review of reviews to capture **non-Cochrane systematic reviews** and meta-analyses which address the gaps identified in the evidence
Step 7	Reference harvesting to **extract the primary studies** from the reviews and meta-analyses identified in steps 1 and 6
Step 8	Named **author** searches
Step 9	Gap search for **named populations or settings**

[1] Cochrane Database of Systematic Reviews

Step 10	Gap search for **aspects of care or delivery**

Consideration will be given to the need and value of conducting steps in grey fill.

The guideline development team will work closely with the Cochrane Tobacco Addiction group (Cochrane TAG) to add value to the evidence reviews. This has included TAG offering access to review update schedules, intelligence on the likelihood that conclusions of reviews currently being updated, access to prepublication reports, expert networks and access to TAG database of trials (useful for steps 2, 4 and 5). The TAG will remain independent of NICE.

A.1.2 Evidence selection and quality appraisal

Methods for evidence review and reporting will conform to The Manual and use experience from preceding PHSC internal guidelines development-led guidelines.

The review of reviews (R0) will aim to provide a brief summary of the key characteristics of the Cochrane systematic reviews. The features of the specification will be broadly similar for reviews 1-3. Review 4 (consumer e-cigarettes) will focus on more descriptive evidence. Review 5 (digital media) will draw on the findings of reviews 1-4, with supplementary inputs from a call for evidence if needed.

The AMSTAR quality appraisal checklist (see Appendix G.1) was used for systematic reviews and the EPOC Checklist (see Appendix G.2) for RCTs, non-randomised controlled trials and controlled before-after studies checklist was used for individual studies. The quality was interpreted as follows;

++ Indicates that for that particular aspect of study design, the study has been designed or conducted in such a way as to minimise the risk of bias

+ Indicates that either the answer to the checklist question is not clear from the way the study is reported, or that the study may not have addressed all potential sources of bias for that particular aspect of study design

- Should be reserved for those aspects of the study design in which significant sources of bias may persist

The final quality ratings are available in Appendix H.

A.1.3 Cost effectiveness reviews

No review of cost effectiveness evidence was undertaken. Instead, a bespoke model was developed which explored the threshold at which interventions are cost effective and assessed the cost effectiveness of a range of interventions identified in the effectiveness reviews.

A.2 Revised methodology and presentation of findings

Towards the end of development, the committee agreed to restructure the evidence reviews to ensure clarity of how the committee discussed the evidence and the expert testimonies presented. This allow for new sections to be added outlining the different consicerations of the committee discussion

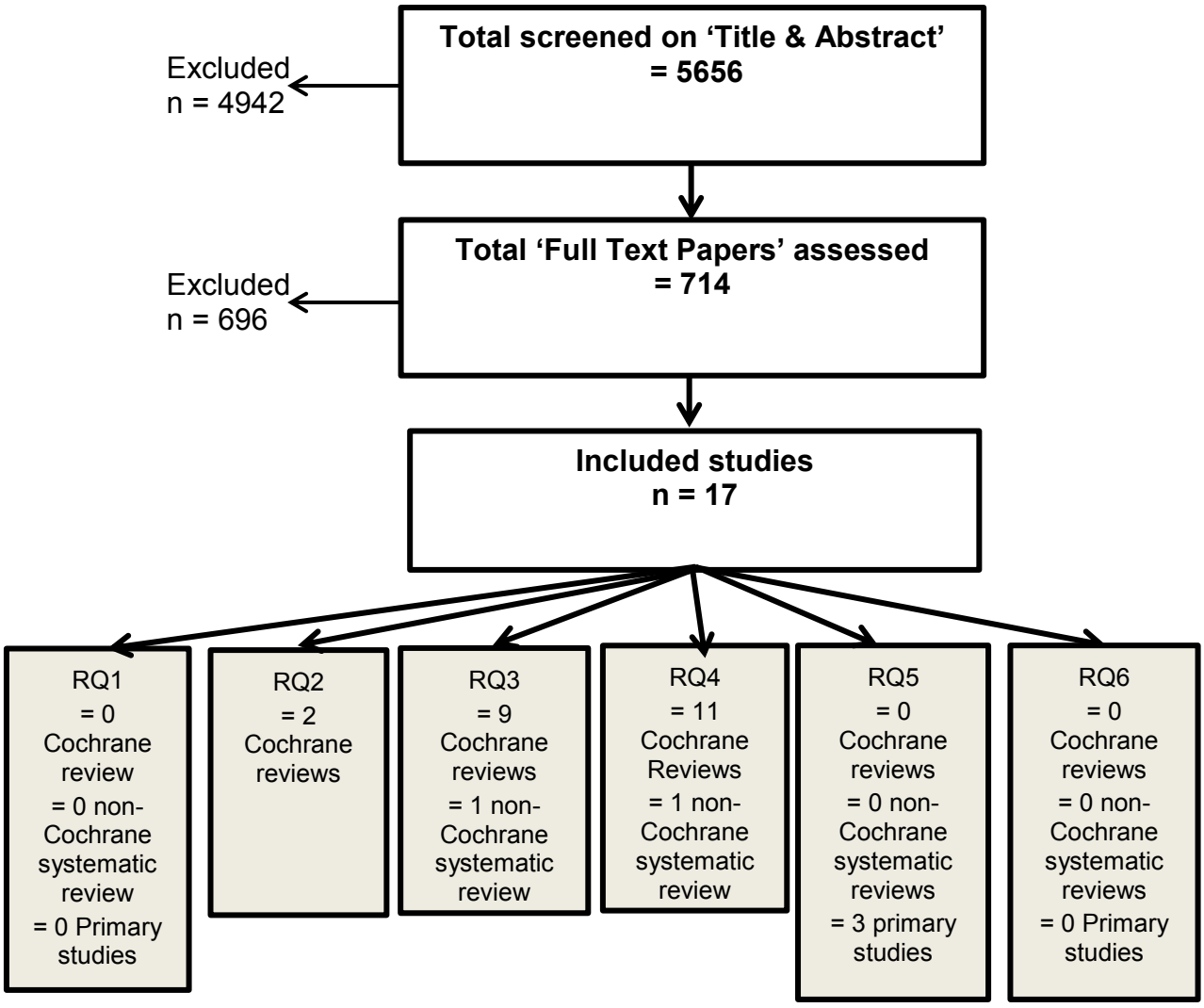
The new sections added are as follows

The committee's discussion of the evidence

- Interpreting the evidence
    - The outcomes that matter most
    - The quality of the evidence
    - Benefits and harms
- Cost effectiveness and resource use
- Other factors the committee took into account

As a result of this restricting the flow of literature through the reviews is summarised in Figure 1.

Figure 1: Flowchart



Appendix B: Review protocols

See separate document here

Appendix C: Search strategy and history

See separate document here

Appendix D: Evidence tables

D.1 Very brief advice

No evidence found for this review.

D.2 Brief advice

Evidence table: Rice et al, 2013

Bibliographic reference	Rice VH, Hartmann-Boyce J, Stead LF. Nursing interventions for smoking cessation. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD001188. DOI: 10.1002/14651858.CD001188.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To determine the effectiveness of nursing-delivered smoking cessation interventions.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialized Register (MEDLINE, EMBASE and PsycINFO) and CINAHL. • Hand-searching of specialist journals, conference proceedings, and reference lists of previous trials and overviews.
	Dates: -June 2013.
	Inclusion/exclusion criteria Included: • Adult smokers (>18yrs). • Either gender • RCTs of smoking cessation interventions delivered by nurses or health visitors • Trials had to have at least two treatment groups. • Allocation to treatment groups must have been stated to be 'random' • Follow up of at least 6 months Excluded: • Trials recruiting only pregnant women. • Trials that did not include data on smoking cessation rates. • Studies comparing advice with advice and NRT. • Studies that used historical controls
	Quality assessment: Risk of bias assessment included: random sequence generation (selection bias), allocation concealment (selection bias), incomplete outcome data assessment (attrition bias) and any other bias. Overall quality of the evidence was assessed using GRADE.
	Number of studies: 49.
Review population and setting	**Details (demographics):** Over 17,000. 18 studies included participants with a diagnosed health problem, given the deliverer and setting.

	Note: Trials in primary care generally did not select participants with a particular health problem.
	Setting: Countries: USA (17), UK (10), Canada (4), Australia (2), China (2), Denmark (2), Japan (2), The Netherlands (2),Norway (2), Spain (2), Belgium (1), South Korea (1) and Sweden (1). One multicenter study was conducted in multiple European countries. Settings: 20 trials intervened with hospitalised participants. 24 studies recruited from primary care or outpatient clinics, one study recruited employees during a workplace health check, 2 enrolled community-based adults motivated to quit, 1 recruited mothers taking their child to a pediatric clinic and 1 recruited people being visited by a home healthcare nurse In some trials, the recruitment took place during a clinic visit whilst in others the invitation to enrol was made by letter. One trial recruited only women and one only men.
Intervention(s)	**Intervention:** • Provision of advice, counselling, and/or strategies to help people quit smoking.
	Comparators: • Usual care, brief advice with a more intensive smoking cessation intervention or different types of interventions.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation. The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Drop-out and losses to follow up was treated as continuing smoker. Where biochemical validation was used, only participants meeting the biochemical criteria for cessation were regarded as abstainers.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis. Risk ratios were used for summarising individual trial outcomes and for the estimate of the pooled effect. The Mantel-Haenszel fixed-effect method was used when appropriate to calculate a weighted average of the RR's of the individual trials, with 95% CI. I^2 was used for statistical heterogeneity and values over 75% indicate a considerable level of heterogeneity.
Results	**Conclusions from systematic review** • The results indicate the potential benefits of smoking cessation advice and/or counselling given by nurses, with reasonable evidence that intervention is effective. The evidence for an effect is weaker when interventions are brief and are provided by nurses whose main role is not health promotion or smoking cessation. The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice so that all patients are given an opportunity to be asked about their tobacco use and to

	be given advice and/or counselling to quit along with reinforcement and follow-up. **Findings from studies. Key comparisons:** • *Comparison: Nursing intervention for smoking cessation vs control or usual care.* 35 studies demonstrated a statistically significant increase in quit rates; risk ratio (RR) of 1.29 with a 95% confidence interval (CI) 1.20 to 1.39 at the longest follow-up. N = 17,629 participants. The point estimate for the pooled effect of the seven lower intensity trials is effectively the same as for the 28 of higher intensity, although for the low-intensity group the confidence interval does not exclude 1 (high-intensity subgroup RR 1.26, 95% CI 1.17 to 1.36, I^2= 54% p<0.00001; low-intensity (10 minutes or less) subgroup RR 1.27, 95% CI 0.99 to 1.62); I^2= 36%, p,0.00001 Participants: N = 13, 613 (high intensity) and 4016 (low intensity). • Pooling 15 trials of cessation interventions for non-hospitalized adults showed an increase in the success rates (RR 1.81, 95% CI 1.48 to 2.22).
Limitations	**Identified by authors** • The distinction used between high and low intensity based on the length of initial contact and number of planned follow-ups may not have accurately distinguished among the key elements that could have contributed to greater efficacy.
	Identified by developers • None.
Additional comments	**Comments** • A reasonable proportion of the studies were conducted in the UK (10/49). • The evidence for non-secondary care settings is relatively small. **Relevance to Recommendations:** • Many of the studies were conducted in secondary care settings, especially those with a focus on a specific (often smoking-related) health problem. However, the direction of effect was consistent in different intensities of intervention, in different settings, and in smokers with and without tobacco-related illnesses. • The results support a modest but positive effect for smoking cessation intervention by nurses, but with caution about the effects that can be expected if interventions are very brief or cannot be consistently delivered. • The availability of smoking cessation advisers in the UK may remove the need for a focus on nurses in primary care settings.
	Source of funding

	Internal Wayne State University College of Nursing, Adult Health & Administration, USA. Department of Primary Health Care, Oxford University, UK. External American Heart Association, USA. NHS Research & Development Programme, UK.

Evidence table: Stead et al, 2013

Bibliographic reference	Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews 2013, Issue 5. Art. No.: CD000165. DOI: 10.1002/14651858.CD000165.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To assess the effectiveness of advice from physicians in promoting smoking cessation; to compare minimal interventions by physicians with more intensive interventions; to assess the effectiveness of various aids to advice in promoting smoking cessation, and to determine the effect of anti-smoking advice on disease-specific and all-cause mortality.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialised register;MEDLINE, EMBASE and PsycINFO and the Cochrane Central Register of Controlled Trials together with hand-searching of specialist journals, conference proceedings, proceedings and reference lists of previous trials and overviews in smoking cessation. Also searched in Latin American databases through BVS which covered 6 databases.
	Dates: -2013
	Inclusion/exclusion criteria Included: • RCTs • Trials where allocation to treatment was by a quasi-randomised method • Cessation assessed at least 6 months after start of intervention • Smokers of either gender Excluded: • Pregnant women • Studies which used historical controls • Comparisons with pharmacotherapies- studies in which participants were randomised to receive advice versus advice plus some form of NRT rather than advice. • Studies of multifactorial lifestyle counselling for example dietary and exercise advice. • Studies without cessation rates
	Quality assessment: Risk of bias assessment included: sequence generation and allocation concealment as markers for the risk of selection bias, and assessment of the level and reporting of incomplete outcome data as a measure of attrition bias.
	Number of studies: 42
Review population and setting	**Details (demographics):** Approx. 31000 smokers in total (31212 participants across 42 studies). In some trials, participants were at risk of specified diseases (chest disease, diabetes, ischaemic heart disease), but most were from unselected populations.

	Setting: Countries: The studies were conducted in a variety of countries including: UK (12), USA (9), Canada (5), Netherlands (2), Australia (2), Germany. Settings: The most common setting for delivery of advice was primary care. Other settings included hospital wards and outpatient clinics, and industrial clinics.
Intervention(s)	**Intervention:** • Physician advice (or supported by another healthcare worker): defined advice 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. • Minimal intervention: single consultation (up to 20 mins) plus one follow-up visit. • Intensive intervention: involved a greater time commitment at the initial consultation, the use of additional materials other than a leaflet, or more than one follow-up visit.
	Comparators: • no advice (or usual care), or compared differing levels of physician advice to stop smoking.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation after at least 6 months follow up. The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Biochemical validated rates used where available. Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis. Where possible, a meta analysis using a Mantel-Haenszel fixed-effect model was performed. They used the I^2 statistic to investigate statistical heterogeneity, a value greater than 50% may be considered substantial heterogeneity.
Results	**Conclusions from systematic review** • The results of this review indicate the potential benefit from brief simple advice given by physicians to their smoking patients. The challenge as to whether or not this benefit will be realised depends on the extent to which physicians are prepared to systematically identify their smoking patients and offer them advice as a matter of routine. Providing follow-up, if possible, is likely to produce additional benefit. However, the marginal benefits of more intensive interventions, including use of aids, are small, and cannot be justified as a routine intervention in unselected smokers. They may, however, be of benefit for individual, motivated smokers. • Assuming an unassisted quit rate of 2 to 3%, a brief advice intervention can increase quitting by a further 1 to 3%. Additional components appear to have only a small effect, though there is a small additional benefit of more

	intensive interventions compared to very brief interventions. **Findings from studies. Key comparisons:** • *Comparison: brief advice (as part of a minimal intervention) versus no advice (or usual care).* The 17 trials of the results demonstrated a statistically significant increase in quit rates; relative risk (RR) 1.66, 95% confidence interval (CI) 1.42 to 1.94. N = 13724 participantsI^2= 31%, p<0.00001 • *Comparison: more intensive intervention versus no advice (or usual care).* The 11 trials of the results demonstrated a statistically significant increase in quit rates; the point estimate was a little larger than for brief advice: RR 1.86, 95% confidence interval (CI) 1.60 to 2.15. N = 8515 participants, I^2=40%, p<0.00001. • *Comparison: brief advice (as part of a minimal intervention) versus more intensive intervention.* The direct comparison between intensive and minimal advice in 15 trials suggested overall that there was a small but significant advantage of more intensive advice (RR 1.37, 95% CI 1.20 to 1.56), with little evidence of heterogeneity (I^2 = 32%) p<0.00001 • The results of the main meta-analyses were not sensitive to exclusion of trials rated at high risk of bias on any single item, or to exclusion of all trials rated at high risk of bias for any item.
Limitations	**Identified by authors** • Only a minority of trials used biochemical measures to confirm self-reports of abstinence.
	Identified by developers • Many of trials were pre-1995. • There was limited reporting of summary study characteristics.
Additional comments	**Comments** • There was a good proportion of UK studies in the review (12/43). **Relevance to Recommendations:** • Most of the studies were conducted in primary care settings, although out-of-scope studies within secondary care were also included. • The evidence relates to physicians and existing recommendations for brief advice and behavioural support. • Re Physician advice: The review results indicate the potential benefits of brief advice. • Re Physician advice: The addition of more intensive interventions may not be justified as routine, unless the individual is motivated to quit.
	Source of funding

	• University of Oxford, Department of Primary Health Care, UK. • National School for Health Research School for Primary Care Research, UK. • NHS Research and Development Programme, UK..

D.3 Behavioural support

Evidence table: Cahill et al, 2010

Bibliographic reference	Cahill K, Lancaster T, Green N. Stage-based interventions for smoking cessation. Cochrane Database of Systematic Reviews 2010, Issue 11. Art. No.: CD004492. DOI: 10.1002/14651858.CD004492.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To test the effectiveness of stage-based interventions in helping smokers to quit.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialized Register (MEDLINE, EMBASE and PsycINFO) and CINAHL. • Hand-searching of specialist journals, conference proceedings and reference lists of previous trials and overviews.
	Dates: -August 2010
	Inclusion/exclusion criteria Included: • RCTS or quasi-RCTs. • Smokers of any age. Excluded: • Studies which measured stage of change but did not modify their intervention in light of it. • Trials with less than 6 months follow up period from the start of treatment.
	Quality assessment: Risk of bias assessment included: adequate sequence generation, allocation concealment, blinding, incomplete outcome data assessment and any other bias.
	Number of studies: 41.
Review population and setting	**Details (demographics):** 33,000 participants. Smokers, any age, race or gender.
	Setting: Countries: USA (21), UK (5), Australia (3), the Netherlands (3), Germany (3), and one in each of Belgium, Canada, Finland, Switzerland, Taiwan and Japan. Settings: Eleven of the included studies were population-based. Nine were set in clinics or in out-patient departments, three in antenatal clinics and three on hospital wards. Five were set in family practices. Six were education-based, including three set in secondary schools, two in colleges and one accessing the parents of school children. Two trials were conducted through telephone quitlines, and two were set in worksites.
Intervention(s)	**Intervention:** • Any intervention using a stage-based design to influence a change in smoking behaviour.

	Comparators: • Non-stage-based control (lower or equal intensity), or with a no-intervention control or usual care group.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation (abstinence from smoking for at least 6 months). The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Preferred biochemically validated rates were reported. Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Results described as a risk ratio with 95% confidence interval and meta-analysis. Where appropriate, meta- analysis was performed to estimate a pooled risk ratio, using the Mantel- Haenszel fixed-effect model. Statistical heterogeneity was assessed using the I^2; values over 50% suggest moderate heterogeneity and over 75% substantial heterogeneity. Risk of bias included; sequence generation, allocation concealment, blinding, incomplete outcome data addressed and other bias.
Results	**Conclusions from systematic review** • Based on four trials using direct comparisons, stage-based self-help interventions (expert systems and/or tailored materials) and individual counselling were neither more nor less effective than their non-stage-based equivalents. Thirty-one trials of stage-based self help or counselling interventions versus any control condition demonstrated levels of effectiveness which were comparable with their non-stage-based counterparts. Providing these forms of practical support to those trying to quit appears to be more productive than not intervening. However, the additional value of adapting the intervention to the smoker's stage of change is uncertain. The evidence is not clear for other types of staged intervention, including interactive computer programmes and training of physicians or lay supporters. The evidence does not support the restriction of quitting advice and encouragement only to those smokers perceived to be in the preparation and action stages. **Findings from studies. Key comparisons:** • *Comparison: stage-based vs generic or non-stage-based intervention of a similar version of comparable intensity:* Two studies contributed and found no clear advantage. Relative risk (RR) was 0.93 (95% confidence interval (CI) 0.62 to 1.39). N = 2117 I^2= 21%, p=0.71. • *Comparison: Staged based vs counselling* (individual, with or without supplementary self-help materials). Two studies contributed to the comparison, returning an RR of 1.00 (95%CI 0.82 to 1.22). N= 1138 I^2= 0%, p= 1.0. • *Comparison: Staged based vs non-staged based versions.* Twelve trials (n=14,446) comparing stage-based self-help with 'usual care' or assessment only gave an RR of 1.32 (95% CI 1.17 to 1.48) analysis not shown. Thirteen trials of stage-based individual counselling versus any control condition gave an RR of 1.24 (95% CI 1.08 to 1.42) analysis not shown.

Limitations	**Identified by authors** • The current evidence base is underpowered and precludes robust conclusions.
	Identified by developers • None
Additional comments	**Comments** • 5 UK studies were included. • Many of the studies were conducted in settings that are out of scope: worksites, antenatal clinics, telephone quit lines. **Relevance to Recommendations:** • Four trials, which directly compared the same intervention in stage-based and standard versions, found no clear advantage for the staging component. This confirms an existing recommendation. • Comparisons between staged based vs usual care are consistent with the proven effectiveness of these interventions in their non-stage-based versions. • Offering practical support to smokers trying to quit delivers higher success rates than 'usual care' or assessing their smoking status, but the additional value of adapting the intervention to the smoker's stage of change is unclear.
	Source of funding Department of Primary Health Care, Oxford University, UK.

Evidence table: Carr & Ebbert, 2012

Bibliographic reference	Carr AB, Ebbert J. Interventions for tobacco cessation in the dental setting. Cochrane Database of Systematic Reviews 2012, Issue 6. Art. No.: CD005084. DOI: 10.1002/14651858.CD005084.pub3
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To assesses the effectiveness of interventions for tobacco cessation delivered by oral health professionals and offered to cigarette smokers and smokeless tobacco users in the dental office or community setting.
Review quality	+
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialized Register (CENTRAL), MEDLINE, EMBASE and PsycINFO) and CINAHL, healthstar, ERIC, NTIS, Dissertation abstracts online, DARE and Web of science.
	Dates: -Nov 2011.
	Inclusion/exclusion criteria Included: • RCTs and pseudo-RCTs. • Cessation assessed at least 6 months after start up. • Tobacco users (including smokeless) - either expressing and interest or no interest to quit. Excluded: • - Trials which did not report tobacco use outcomes or did not have sufficiently long follow-up were excluded
	Quality assessment: Risk of bias assessment included: random sequence generation, allocation concealment and attrition bias. The control of detection

	bias through the blinding of participants or oral health personnel was limited due to the nature of the behavioural interventions evaluated.
	Number of studies: 14 (6 studies covered smokeless tobacco only). 8 studies evaluated interventions among cigarette smokers, 6 of which involved adult smokers in dental practice settings.
Review population and setting	**Details (demographics):** 10535 participants. Any age.
	Setting: Countries: US (12), UK (1), Sweden (1). Settings: Dental office or community setting. 6 studies were conducted in private practice office settings, 1 study involved community public health dental clinics, 1 was set in a hospital-based periodontal clinic, 2 took place in managed care clinics, 1 took place in military clinics. 3 involved oral health professionals (dentists and dental hygienists) providing interventions to athletes within high school or college community settings.
Intervention(s)	**Intervention:** • Any intervention to promote tobacco use cessation which included a component delivered by a dentist, dental hygienist, dental assistant or office staff in the dental practice setting and any combination of these. • Brief advice to quit, provision of self-help materials, counselling, pharmacotherapy or any combination of these, or referral to other sources of support.
	Comparators: • Usual care or placebo, and/or intervention versus other intervention.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was smoking cessation (and tobacco use). The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (odds ratio) and meta-analysis. The effect was summarised as an odds ratio, with correction for clustering where appropriate. Heterogeneity was assessed using the I^2 statistic and where appropriate a pooled effect was estimated using an inverse variance fixed-effect model. Analysis of smokeless tobacco users was presented separately.
Results	**Conclusions from systematic review** • Available evidence suggests that behavioural interventions for tobacco cessation conducted by oral health professionals incorporating an oral examination component in the dental office or community setting may increase tobacco abstinence rates among both cigarette smokers and smokeless tobacco users. Differences between the studies limit the ability to make conclusive recommendations regarding the intervention components that should be incorporated into clinical practice, however, behavioural counselling (typically brief) in conjunction with an oral examination was a consistent intervention component that was also provided in some control groups.

	Findings from studies. Key comparisons: • *Comparison: behavioural counselling (typically brief) in conjunction with an oral examination vs control.* Pooling all 14 studies (10535 participants) suggested that interventions conducted by oral health professionals can increase tobacco abstinence rates (odds ratio [OR] 1.71, 95% confidence interval [CI] 1.44 to 2.03), p<0.00001, at six months or longer, but there was evidence of heterogeneity (I^2 = 61%). Within the subgroup of interventions for smokers (8 studies of 7294 partcipants), heterogeneity was smaller (I^2 = 51%),OR 1.74, 95% CI 1.33 to 2.27,p= 0.000058, but was largely attributable to a large study showing no evidence of benefit. Within this subgroup there were 5 studies which involved adult smokers in dental practice settings. Pooling these showed clear evidence of benefit and minimal heterogeneity (OR 2.38, 95% CI 1.70 to 3.35, I^2 = 3%, p<0.00001) but this was a posthoc subgroup analysis.
Limitations	**Identified by authors** • Insufficient evidence exists to make conclusions about the effectiveness of specific intervention components.
	Identified by developers • Biochemical confirmation was used to validate self report in only 2 studies. • Limited to dental setting.
Additional comments	**Comments** • Evidence included smokeless tobacco, although subgroup interventions were considered for smokers. • One UK study was included. **Relevance to Recommendations:** • The authors acknowledge that the results should be viewed cautiously, due to the quality of the studies, the insufficient number of studies and differences between the studies limiting conclusiveness about the intervention components. • An insufficient number of studies are available to determine what specific assistance measures delivered by a dental professional provide additional effectiveness beyond brief advice. However, this is in-line with existing guideline PH10 rec 6.
	Source of funding No internal funding External funding: National Institute for Dental and Craniofacial Research, USA.

Evidence table: Huibers et al, 2007

Bibliographic reference	Huibers MJ, Beurskens A, Bleijenberg G, van Schayck CP. Psychosocial interventions by general practitioners. *Cochrane Database of Systematic Reviews* 2007, Issue 3. Art. No.: CD003494. DOI: 10.1002/14651858.CD003494.pub2
Review design	Cochrane Systematic Review
Aim of review	To examine the effectiveness of psychosocial interventions by general practitioners by assessing the clinical outcomes and the methodological quality of selected studies.
Review quality	++
Review search parameters	**Sources** • The Cochrane Collaboration Depression Anxiety and Neurosis group Controlled Trials Registers (CCDANCTR-Studies and CCDANCTR-References) including The Cochrane Library, CINAHL, E,BASE, LILACS, MEDLINE, NRR, PSYCLIT, PSYCHINFO, PSYNDEX and SIGLE. • Citation tracking and personal communication with experts.
	Dates: -October 2005
	Inclusion/exclusion criteria Included: • RCTs, CCTs and controlled patient preference trials. • Psycho-social interventions delivered by GPs. At least 2 face contacts and psychological process is central. • All languages Excluded: • Psycho-pharma interventions. Or where the Psychosocial interventions could not be evaluated. • The GP was not central - results were not presented for the GP. • Single session interventions • Psychosocial interventions were only delivered in combination with other types of treatment eg. Placebo, pharmacotherapy, physio, and the effectiveness of the psychosocial interventions alone could not be evaluated.
	Quality assessment: using the Maastricht-Amsterdam Criteria List (MACL). MACL contains 17 items to assess internal validity (e.g. selection bias, performance bias, attrition bias and detection bias, 10 items), external validity (descriptive criteria, five items) and statistical aspects (two items). For the qualification of methodological quality (high or low) the 10 MACL items on internal validity were used.
	Number of studies: 10 (2 related to smoking cessation - only these are reported below)
Review population and setting	**Details (demographics):** 1123 participants (Smokers). No restrictions on the type of participants.
	Setting: Countries: N/R. Settings: GP settings/practice.
Intervention(s)	**Intervention:**

	• Psychosocial interventions delivered by GPs. At least 2 face contacts and psychological process is central.
	Comparators: • Usual care or another experimental intervention.
Outcomes and methods of analysis	**Outcomes:** Abstinence at 6 and 12 month follow-up..
	Methods of analysis: Narrative summary. Evaluation of confidence intervals revealed statistical heterogeneity and abstinence rates were not pooled. Relative risks were calculated for dichotomous outcomes and weighted mean differences for continuous outcomes. In addition to meta-analysis, number needed to treat to benefit or harm were calculated for the last available endpoint if outcomes were presented as dichotomous data.
Results	**Conclusions from systematic review** • In general, there is little available evidence on the use of psychosocial interventions by general practitioners. Of the psychosocial interventions reviewed, problem-solving treatment for depression may offer promise, although a stronger evidence-base is required and the effectiveness in routine practice remains to be demonstrated. • There is conflicting evidence that counselling by a GP is more or no less effective than minimal intervention on smoking behaviour. There is limited evidence that counselling by a GP is no less effective than counselling plus nicotine gum or counselling plus spirometry by a GP on smoking behaviour. **Findings from studies. Key comparisons:** • In one high-quality study, the effects of five-session 'repeated counselling' (RC) delivered by one of 44 GPs were no different compared to the effects of a one-session minimal intervention (MI), repeated counselling plus nicotine gum RC+gum) or repeated counselling plus spirometry (RC+spiro): biochemically validated smoking abstinence rates at 12 month follow-up were respectively 4.8%, 5.5%, 7.5%, and 6.5%. • In one low-quality study (Richmond 1985), six-session smoking cessation counselling delivered by one of three GPs was superior to a minimal intervention (usual care and use of a diary) consisting of two sessions: at 6 month follow-up, 33% of the patients in the counselling group were biochemically validated as abstinent from smoking versus 3% in the minimal intervention group.
Limitations	**Identified by authors** • The authors used a conservative definition of 'psychosocial interventions' which affected the inclusion of studies.
	Identified by developers • The central focus was psychosocial interventions rather than smoking cessation per se. Therefore the usual focus on biochemical validation and allocation for non-completion was not central to the review, although relevant information was reported. The review had limited overall relevance to the area of interest.

	• Details of the individual scores for the risk of bias MACL were not presented in the report. • Only 2 studies included participants who were smokers and applicable to the review.
Additional comments	**Comments** • Both smoking cessation studies were conducted before 1991. • If more than one outcome measure was reported, the outcome measures that were believed to be the main outcome measures were analysed **Relevance to Recommendations:** • The included studies are pre-1991 and the applicability uncertain. • Although the evidence was equivocal, it remains to be seen whether related smoking cessation interventions would be delivered by GPs or another provider in a UK setting - especially in respect of time and costs.
	Source of funding Health Research and Development Council (ZorgOnderzoek Nederland), Netherlands.

Evidence table: Lancaster & Stead, 2017(Individual counselling)

Bibliographic reference	Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews2017, Issue 3. Art. No.: CD001292. DOI: 10.1002/14651858.CD001292.pub3.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To determine the effects of individual counselling.
Review quality	+
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group Specialized Register. Previous reviews and meta-analyses, including all studies in the previous US guidelines.
	Dates: -May 2016
	Inclusion/exclusion criteria Included: • RCTs and quasi-RCTs. • Cessation assessed at 6 months after start of intervention.(minimum follow up of 6 months) • One treatment arm consisted of an unconfounded intervention from a counsellor. Excluded: • Trials recruiting only pregnant women • Trials recruiting only children and adolescents. • Counselling delivered by doctors and nurses as part of clinical care • Interventions which address multiple risk factors in addition to smoking.
	Quality assessment: Risk of bias assessment included: four domains of study quality; randomisation sequence generation; sequence concealment, blinding during treatment and follow up; and incomplete outcome data.
	Number of studies: 49.
	Details (demographics): Over 19000 participants. Any smokers (except pregnant women).

Review population and setting	A common setting for delivery of advice was secondary care, therefore many of the participants were hospital in- or outpatients.
	Setting: Countries: The vast majority of studies were conducted in USA (30 of 49). Other countries included UK (2), Denmark (3), Spain (3), Australia (2), Germany, Switzerland, Sweden, Hong Kong, ChinaS. Korea, Japan, Netherlands and India. Settings: 19 of 49 studies recruited in in-patient settings (out of scope). Other studies recruited a mixture of primary and community settings. 2 studies recruited only women.
Intervention(s)	**Intervention:** • Individual counselling as a face-to-face encounter between a smoking patient and a counsellor trained in assisting smoking cessation.
	Comparators: • No advice (or usual care) or less intensive counselling interventions. • Individual counselling versus no treatment, brief advice or self-help materials • More intensive versus less intensive individual counselling • Comparisons between counselling methods matched for contact time.
Outcomes and methods of analysis	**Outcomes:** • Abstinence (at least six months after start of treatment); used sustained abstinence, or multiple prevalence where available. • The most rigorous definition of abstinence was used in each trial. • With or without biochemically validated rates. • Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis, where appropriate. Individual study results summarised as a risk ratio. Where appropriate a Mantel-Haenszel fixed effect method to estimate a pooled risk ration with 95% CI.
Results	**Conclusions from systematic review** • The review looked at trials of counselling by a trained therapist providing one or more face-to-face sessions, separate from medical care. All the trials involved sessions of more than 10 minutes, with most also including further telephone contact for support. The review found that individual counselling could help smokers quit, but there was not enough evidence about whether more intensive counselling was better. **Findings from studies. Key comparisons:** • *Comparison individual counselling vs minimal contact (usual care to up to 10 minutes of advice).* Thirty-three trials compared individual counselling to a minimal behavioural intervention. Individual counselling was more effective than control. The relative risk (RR) for smoking cessation at long-term follow up was 1.48, 95% confidence interval (CI) 1.34 to 1.64, $p<0.00001$. $I^2=46\%$ N = 13762 participants.

	• *Comparison individual counselling vs control (no systematic pharmacotherapy).* The subgroup of twenty-seven trials compared individual counselling to a control group (without pharmacotherapy). Individual counselling was more effective than control. The relative risk (RR) for smoking cessation at a long-term follow up was 1.57, 95% confidence interval (CI) 1.40 to 1.77, p<0.00001, I^2= 50% N = 11100 partcipants. • *Comparison: Counselling plus pharmacotherapy vs pharmacotherapy alone*. N= 2662, 6 trials. The subgroup of six studies where counselling was tested as an adjunct to nicotine replacement therapy or bupropion had a smaller estimated effect which just reached significance (RR 1.24; 95% CI 1.01 to 1.51).I^2=0%, p=0.04. • *Comparison more intensive counselling vs brief counselling.* In an analysis combining eleven studies, there was some evidence of benefit from more intensive compared to brief counselling (RR 1.29; 95% CI 1.09 to 1.53). n=2920 I^2= 48%. • *Comparison more intensive counselling vs brief counselling (no pharmacotherapy)* The subgroup of four trials compared more intensive counselling with brief counselling without pharmacotherapy and found no difference between the groups. RR 1.42 95% CI 0.98 to 2.06, N = 872 • *Comparison more intensive counselling vs brief counselling (adjunct to pharmacotherapy).* The subgroups analysis of 8 trials found some benefit with more intensive counselling compared to brief counselling when adjunct to pharmacotherapy. RR 1.26 95% CI 1.04 to 1.52, N = 2048
Limitations	**Identified by authors** • The review was not able to identify the most effective intensity and duration of intervention for different populations.
	Identified by developers • Overall, description of methods and analysis was limited.
Additional comments	**Comments** • Lack of interest in quitting was not an explicit exclusion criteria in any study, but the level of motivation to quit smoking was sometimes difficult to assess. **Relevance to Recommendations:** • Various studies included secondary care patients and (to a lesser degree) worksites. It is not clear whether lower intensity (even brief advice) is more or less effective in primary and community settings from this evidence. The authors do state 'Almost half the trials recruited people in hospital settings, but there was no evidence of heterogeneity of results in different settings'. • The review included only 2 UK studies. • The review indicates that intensive counselling (more than 10 minutes) is more effective than brief advice.
	Source of funding Internal Oxford University Department of Primary Health Care, UK.

	National Institute for Health Research School for Primary Care Research, UK. External NHS Research and Development Programme, UK.

Evidence table: Lindson-Hawley et al, 2015

Bibliographic reference	Lindson-HawleyN,ThompsonTP, Begh R.Motivational interviewing for smoking cessation. CochraneDatabase of Systematic Reviews 2015, Issue 3. Art. No.: CD006936. DOI: 10.1002/14651858.CD006936.pub3.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To determine whether or not motivational interviewing (MI) promotes smoking cessation.
Review quality	+
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialized Register (MEDLINE, EMBASE and PsycINFO) and CINAHL. • Hand-searching of specialist journals, conference proceedings and reference lists of previous trials and overviews.
	Dates: -August 2014
	Inclusion/exclusion criteria Included: • RCTs, cluster-RCTs • Cessation assessed at least 6 months after start up (minimum follow up of 6 months from start of treatment). Excluded: • Trials recruiting only pregnant women or adolescents who smoked. • Stage-based interventions (covered by Cahill 2010) • Trials not including data on smoking cessation
	Quality assessment: Risk of bias assessment included: randomisation procedure, allocation concealment, incomplete outcome data assessment and any other bias. GRADE was used to assess the quality of the evidence for the primary outcome across the included studies.
	Number of studies: 28.
Review population and setting	**Details (demographics):** 16,000 participants. Tobacco users of either gender.
	Setting: Countries:. USA (23), UK (1), Spain (1), Brazil (1), Sweden (1), South Africa (1). Recruited in any setting, Settings: 4 were set in primary care clinics, 1 in participants' homes, and 3 were delivered through telephone quitline services. Three programmes were provided through screening clinics, 6 in specialist outpatient clinics, 6 in hospitals/inpatient settings, 3 in university or laboratory settings and 2 in military settings.
Intervention(s)	**Intervention:** • Trials that make explicit reference to MI principles and comply with MI principles and practice in the opinion of the authors. • MI interventions may include pharmacotherapy - provided it was not the intervention being tested. • Interventions based on individual or group arrangement. • Face to face or telephone based interviews

	• Any healthcare professional or counsellor
	Comparators: • Usual care, brief advice (ranging from 2 to 15 minutes) and other therapies.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation. The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis. I^2 was used for statistical heterogeneity.A value greater than 50% may be considered to represent substantial heterogeneity. Estimate pooled treatment effects as risk ratios, using the Mantel- Haenszel fixed-effect model. Where biochemical validation was used, regard only those participants meeting the biochemical criteria for cessation as abstainers. Where possible we have extracted smoking outcomes as continuous abstinence but also accepted point prevalence. ITT analysis for missing data.
Results	**Conclusions from systematic review** • Motivational interviewing may assist people to quit smoking. However, the results should be interpreted with caution, due to variations in study quality, treatment fidelity, between-study heterogeneity and the possibility of publication or selective reporting bias. **Findings from studies. Key comparisons:** • *Comparison: MI versus brief advice or usual care*: The overall effect across all 28 included trials, using the strictest definition of abstinence and longest follow-up, gives a modestly significant effect (risk ratio (RR) 1.26; 95% confidence interval (CI) 1.16 to 1.36. I^2= 49% p<0.00001 N = 16,803 participants. • The 16 trials which biochemically validated their outcomes delivered a lower risk ratio (1.12; 95% CI 0.98 to 1.29; N = 7858; I^2 = 29%), which did not reach significance (analyses not shown in paper). • *Comparison: Sub-group analysis by type of therapists*. MI delivered by general practitioners had a larger effect (RR 3.49; 95% CI 1.53 to 7.94: 2 trials, N = 736; I^2 = 27% p=0.0029) when compared with nurses (RR 1.24; 95%CI 0.91 to 1.68; 5 trials, N= 2256; I^2 = 0%, p=0.17) or counsellors (RR 1.25; 95% CI 1.15 to 1.36; 22 trials, N = 13,593; I^2 = 52%,p<0.00001 • *Comparison: Sub-group analysis by number of sessions*. Interventions delivered in a single session (RR 1.26; 95% CI 1.15 to 1.40; 16 trials, N = 12,103; I^2 = 43% p<0.00001;) had a similar effect size to multiple session interventions (RR 1.20; 95% CI 1.02 to 1.42; 11 trials, N = 3928; I^2 = 56%p=0.03 • *Comparison*: Duration of session. Pooling studies in which the MI sessions lasted less than 20 minutes produced a significant, larger effect (RR 1.69; CI 95% 1.34 to 2.12; 9 trials, N= 3651; I^2= 27%,

	p<0.00001. Studies with MI sessions lasting longer than 20 minutes produced a smaller effect (RR 1.20; 95% CI 1.08 to 1.32; 16 trials, N= 10,306; I^2= 56%; p=0.00039.
Limitations	**Identified by authors** • Funnel plot suggest a measure of publication bias or selective reporting or both, in favour of positive findings, which may compromise the strength of the evidence and the reviews conclusions.
	Identified by developers • Little detail given on the MI technique- most studies merely specified that the intervention was carried out according to established MI techniques. • All but one of the trials reported point prevalence as a main outcome. • This review includes studies of participants using smokeless tobacco, with 2 studies recruiting only smokeless tobacco users.
Additional comments	**Comments** • Only 4 studies were conducted in primary care settings. • Only one study was conducted in the UK. **Relevance to Recommendations:** • The overall effect of MI compared to brief or usual care was modest. There is limited evidence that GPs confer greater benefit than those delivered by nurses or counsellors. • When delivered by nurses the effect was non-significant (see also Rice 2013). • MI was conducted in 1 to 6 sessions (duration ranging from 10-60 minutes). • The effect of shorter sessions (<20 mins) appear to be higher.
	Source of funding Internal University of Oxford, UK. Computer and database use, University of Plymouth, UK No external sources.

Evidence table: Mdege et al 2014

Bibliographic reference	Mdege N D, and Chindove S. 2014. "Effectiveness of tobacco use cessation interventions delivered by pharmacy personnel: A systematic review". Research in Social & Administrative Pharmacy 10:21-44.
Review design	Systematic Review (narrative summary)
Aim of review	This review aimed to identify, describe and synthesis currently available evidence on the effectiveness of tobacco use cessation interventions delivered by pharmacy personnel.
Review quality	+
Review search parameters	**Sources** • MEDLINE, EMBASE, PSYCINFO, Cochrane Library, Web of Knowledge and the Current Controlled Trials Register.

	Dates: up until May 2012
	Inclusion/exclusion criteria Included: • Controlled clinical trials (CCTs), cluster randomised controlled trials (CCRTs) and randomized controlled trials (RCTs), which were comparing any pharmacy personnel delivered tobacco use cessation intervention to no treatment, usual care or other active treatments Excluded: • None reported
	Quality assessment: Study quality assessment included adequacy of sequence generation and allocation concealment, sample size/power calculation, blinding, handling of incomplete data, follow-up rates, use of intention to treat.
	Number of studies: 10
Review population and setting	**Details (demographics):** N=20,133
	Setting*: Awaiting retrieval of supplementary material prior to presenting these findings* Countries: 3 for UK and USA, and 1 each for Canada, Denmark, Japan and Australia. Settings: Mixed
Intervention(s)	**Intervention:**
	Comparators: Usual care
Outcomes and methods of analysis	**Outcomes:** Abstinence (e.g., point prevalence; continuous abstinence) and relapse (e.g., time to relapse) as measured by the respective studies.
	Methods of analysis: Narrative summary
Results	**Conclusions from systematic review** The findings from this systematic review suggest that pharmacy personnel delivered non- pharmacological tobacco use cessation interventions offering behavioral counselling or support, and those combining these non-pharmacological interventions with NRT/pharmacological approaches, are potentially effective. Evidence on pharmacy personnel delivered NRT interventions is mixed. However, these findings are based on a very limited number of studies, and hence more evidence in needed before more robust conclusions can be made.
Limitations	**Identified by authors** There were limitations on the quality of the studies included in this review, particularly on. sample size calculation, sequence generation, allocation concealment, and ensuring and verifying intervention fidelity for non-pharmacological interventions.
	Identified by developers None
Additional comments	**Comments** **Relevance to Recommendations:** • The overall beneft=it of pharmacy delivered interve tions was not clear.
	Source of funding Internal sources:

	None reported

Evidence table: Rice et a. 2013

Bibliographic reference	Rice VH, Hartmann-Boyce J, Stead LF. Nursing interventions for smoking cessation. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD001188. DOI: 10.1002/14651858.CD001188.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To determine the effectiveness of nursing-delivered smoking cessation interventions.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group specialized Register (MEDLINE, EMBASE and PsycINFO) and CINAHL. • Hand-searching of specialist journals, conference proceedings, and reference lists of previous trials and overviews.
	Dates: -June 2013.
	Inclusion/exclusion criteria Included: • Adult smokers (>18yrs). • Either gender • RCTs of smoking cessation interventions delivered by nurses or health visitors • Trials had to have at least two treatment groups. • Allocation to treatment groups must have been stated to be 'random' • Follow up of at least 6 months Excluded: • Trials recruiting only pregnant women. • Trials that did not include data on smoking cessation rates. • Studies comparing advice with advice and NRT. • Studies that used historical controls
	Quality assessment: Risk of bias assessment included: random sequence generation (selection bias), allocation concealment (selection bias), incomplete outcome data assessment (attrition bias) and any other bias. Overall quality of the evidence was assessed using GRADE.
	Number of studies: 49.
Review population and setting	**Details (demographics):** Over 17,000. About 18 studies included participants with a diagnosed health problem, given the deliverer and setting. Note: Trials in primary care generally did not select participants with a particular health problem.
	Setting: Countries: USA (17), UK (10), Canada (4), Australia (2), China (2), Denmark (2), Japan (2), The Netherlands (2),Norway (2), Spain (2), Belgium (1), South

	Korea (1) and Sweden (1). One multicenter study was conducted in multiple European countries. Settings: 20 trials intervened with hospitalised participants. 24 studies recruited from primary care or outpatient clinics, one study recruited employees during a workplace health check, 2 enrolled community-based adults motivated to quit, 1 recruited mothers taking their child to a pediatric clinic and 1 recruited people being visited by a home healthcare nurse In some trials, the recruitment took place during a clinic visit whilst in others the invitation to enrol was made by letter. One trial recruited only women and one only men.
Intervention(s)	**Intervention:** • Provision of advice, counselling, and/or strategies to help people quit smoking.
	Comparators: • Usual care, brief advice with a more intensive smoking cessation intervention or different types of interventions.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation. The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence.Drop-out and losses to follow up was treated as continuing smoker. Where biochemical validation was used, only participants meeting the biochemical criteria for cessation were regarded as abstainers.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis. Risk ratios were used for summarising individual trial outcomes and for the estimate of the pooled effect. The Mantel- Haenszel fixed-effect method was used when appropriate to calculate a weighted average of the RR's of the individual trials, with 95% CI. I^2 was used for statistical heterogeneity and values over 75% indicate a considerable level of heterogeneity.
Results	**Conclusions from systematic review** • The results indicate the potential benefits of smoking cessation advice and/or counselling given by nurses, with reasonable evidence that intervention is effective. The evidence for an effect is weaker when interventions are brief and are provided by nurses whose main role is not health promotion or smoking cessation. The challenge will be to incorporate smoking behaviour monitoring and smoking cessation interventions as part of standard practice so that all patients are given an opportunity to be asked about their tobacco use and to be given advice and/or counselling to quit along with reinforcement and follow-up. **Findings from studies. Key comparisons:** • *Comparison: Nursing intervention for smoking cessation vs control or usual care.* 35 studies demonstrated a statistically significant increase in quit rates; risk ratio (RR) of 1.29 with a 95% confidence interval (CI) 1.20 to 1.39 at the longest follow-up. N = 17,629 participants. • The point estimate for the pooled effect of the seven lower intensity trials is effectively the same as for the 28 of higher intensity, although for the low-intensity group the confidence

	interval does not exclude 1 (high-intensity subgroup RR 1.26, 95% CI 1.17 to 1.36, I^2= 54% p<0.00001; low-intensity (10 minutes or less) subgroup RR 1.27, 95% CI 0.99 to 1.62); I2= 36%, p,0.00001 Participants: N = 13, 613 (high intensity) and 4016 (low intensity). • Pooling 15 trials of cessation interventions for non-hospitalized adults showed an increase in the success rates (RR 1.81, 95% CI 1.48 to 2.22).
Limitations	**Identified by authors** • The distinction used between high and low intensity based on the length of initial contact and number of planned follow-ups may not have accurately distinguished among the key elements that could have contributed to greater efficacy.
	Identified by developers • None.
Additional comments	**Comments** • A reasonable proportion of the studies were conducted in the UK (10/49). • The evidence for non-secondary care settings is relatively small. **Relevance to Recommendations:** • Many of the studies were conducted in secondary care settings, especially those with a focus on a specific (often smoking-related) health problem. However, the direction of effect was consistent in different intensities of intervention, in different settings, and in smokers with and without tobacco-related illnesses. • The results support a modest but positive effect for smoking cessation intervention by nurses, but with caution about the effects that can be expected if interventions are very brief or cannot be consistently delivered. • The availability of smoking cessation advisers in the UK may remove the need for a focus on nurses in primary care settings.
	Source of funding Internal Wayne State University College of Nursing, Adult Health & Administration, USA. Department of Primary Health Care, Oxford University, UK. External American Heart Association, USA. NHS Research & Development Programme, UK.

Evidence table: Stanton & Grimshaw, 2013

Bibliographic reference	Stanton A, Grimshaw G. Tobacco cessation interventions for young people. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No.: CD003289. DOI: 10.1002/14651858.CD003289.pub5.
Review design	Cochrane Systematic Review (with meta analysis)

Aim of review	To evaluate the effectiveness of strategies that help young people to stop smoking tobacco.
Review quality	++
Review search parameters	**Sources** • Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and PsyclNFO, grey lit, authors. Reference lists of identified studies, manufacturers of smoking cessation products.
	Dates: -2013
	Inclusion/exclusion criteria Included: • RCTs (14), C-RCTs (12) and Controlled trials (2) • Young people who are regular tobacco smokers (<20 years). 'Regular' is smoking on average at least one cigarette a week, and has done so for at least 6 months. Excluded: • Pregnant women • Prevention of uptake programmes • Any programme aimed primarily at the adult population.
	ity assessment: Risk of bias assessment included: sequence generation and allocation concealment as markers for the risk of selection bias, and assessment of the performance, detection bias and attrition. GRADE was used for quality of evidence
	Number of studies: 28
Review population and setting	**Details (demographics):** Approx. 6000 young people in total (across 28 studies).
	Setting: Countries: The studies were conducted in: US (n=24), UK, Australia, Russia, Canada. Settings: Any, including school, hospital, doctor's surgery, dentist.
Intervention(s)	**Intervention:** • Any interventions; these could include pharmacotherapy, psychosocial interventions and complex programmes targeting families, schools or communities. • A range of interventions were apparent in studies: Many studies combined components from various theoretical backgrounds to form complex interventions. The majority used some form of motivational enhancement combined with psychological support such as cognitive behavioural therapy (CBT) and some were tailored to stage of change using the transtheoretical model (TTM). Analyses focused on studies including Transtheoretical Model of change (4 studies); Interventions including motivational enhancement (12 studies); Not on Tobacco (NoT) programmes (6 studies).
	Comparators: • no intervention; delayed intervention beyond the last date of data acquisition including follow-up; information on stopping smoking (brief intervention); general tobacco education.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was smoking status at six months follow-up or longer. 14 studies used biochemical verification.

	Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect and meta-analysis (as outlined in the methods for the Cochrane collaboration). If statistical pooling was not possible findings were presented in narrative form. Where meta-analysis was appropriate, they estimated pooled risk ratios using a Mantel- Haenszel fixed-effect model, based on the quit rates at longest follow up.
Results	**Conclusions from systematic review** • Complex approaches show promise, with some persistence of abstinence (30 days point prevalence abstinence or continuous abstinence at six months), especially those incorporating elements sensitive to stage of change and using motivational enhancement and CBT. Given the episodic nature of adolescent smoking, more data is needed on sustained quitting. There were few trials with evidence about pharmacological interventions (nicotine replacement and bupropion), and none demonstrated effectiveness for adolescent smokers. There is not yet sufficient evidence to recommend widespread implementation of any one model. There continues to be a need for well-designed adequately powered randomized controlled trials of interventions for this population of smokers. **Findings from studies. Key comparisons:** • *Comparison: Trans Theoretical Model vs standard care or dietary advice.* The 3 trials achieved moderate long-term success, with a pooled risk ratio (RR) of 1.56 at one year (95% confidence interval (CI) 1.21 to 2.01). N =1662 participants.I^2- 0%, p=0.00051 • *Comparison: Interventions including motivational enhancement vs brief interventions for smoking cessation:* The 12 trials that included some form of motivational enhancement gave an estimated RR of 1.60 (95% CI 1.28 to 2.01). N= 2667 participants.I^2= 0%, p= 0.000039. GRADE quality: moderate • None of the 13 individual trials of complex interventions that included cognitive behavioural therapy achieved statistically significant results, and results were not pooled due to clinical heterogeneity. • *Comparison: Not on Tobacco (NoT) programmes for smoking cessation in young people vs brief intervention.* There was a marginally significant effect of pooling six studies of the Not on Tobacco programme (RR of 1.31, 95% CI 1.01 to 1.71), although three of the trials used abstinence for as little as 24 hours at six months as the cessation outcome. N = 1420 participants.I^2= 0% p=0.041. GRADE quality low. • Four studies utilise ICTs to deliver part of the intervention. The results were not pooled: 2 studies detected significant evidence of an effect, whereas the other 2 studies did not detect a significant difference between intervention and control arms. • A small trial testing nicotine replacement therapy did not detect a statistically significant effect. Two trials of bupropion, one testing

	two doses and one testing it as an adjunct to NRT, did not detect significant effects. Studies of pharmacotherapies reported some adverse events considered related to study treatment, though most were mild, whereas no adverse events were reported in studies of behavioural interventions.
Limitations	**Identified by authors** • Definitions of quitting (based on point prevalence) used in the studies may not be appropriate for younger smokers with irregular habits. • The majority of studies were judged to be at unclear or high risk of bias in at least one domain. • Losses to follow up ranged from less than 10% to more than 50% of the cohort.
	Identified by developers • Multicomponent interventions so it is difficult to determine which aspect is contributing to effect.
Additional comments	**Comments** • Only 1 UK study was included and focused on the school setting. The majority of studies (24/28) were from USA. • With the exception of 2 small trials, all studies were published in the past 12 years. • Most of the studies were school-based. **Relevance to Recommendations:** • Most of the studies were conducted in a school setting with limited applicability to the focus of the guideline. • There is limited evidence on effectiveness of pharmacotherapies in young people. None demonstrated effectiveness. • The studies based on complex approaches (including motivational enhancement) were noted as showing promise. The need for face-to-face intervention may affect costs.
	Source of funding NR.

Evidence table: Stead & Lancaster 2017(Group therapy)

Bibliographic reference	Stead LF, Carroll AJ, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database of Systematic Reviews 2017, Issue 3. Art. No.: CD001007. DOI: 10.1002/14651858.CD001007.pub3.
Review design	Systematic Review (with meta analysis)
Aim of review	To determine the effects of smoking cessation programmes delivered in a group format compared to self-help materials, or to no intervention; to compare the effectiveness of group therapy and individual counselling; and to determine the effect of adding group therapy to advice from a health professional or to nicotine replacement. To determine whether specific components increased the effectiveness of group therapy. We aimed to determine the rate at which offers of group therapy are taken up.
Review quality	++
	Sources

Review search parameters	• Cochrane Tobacco Addiction Group Trials Register, MEDLINE and PsycINFO, US Public Health Service Clinical Practice Guidelines on smoking cessation
	Dates 1996-2008; -2008
	Inclusion/exclusion criteria Included: • Trials with random allocation of participants. • Minimum of 2 group meetings and follow up of at least 6 months after the start of programme • Group behavioural intervention, such as information, advice and encouragement or cognitive behavioural therapy (CBT) delivered over at least two sessions • Studies which randomised therapists, rather than therapists, to offer group therapy were included provided that the specific aim of the study was to examine the effect of group therapy on smoking cessation. Excluded: • Pregnant women in antenatal care • Trials to prevent relapse, • Trials in which group therapy was provided to both active therapy and placebo arms of trials of pharmacotherapies, unless they had a factorial design. • Studies that primarily investigated the efficacy of aversive smoking, acupuncture, hypnotherapy, exercise or partner support. • Trials in which smokers received group therapy in addition to active or placebo pharmacotherapy unless they had other relevant arms.
	Quality assessment Risk of bias assessment included: adequate sequence generation, allocation of concealment and incomplete outcome data.
	Number of studies 66
Review population and setting	**Details (demographics)** Either gender Number of participants reported below for each comparison.
	Setting: Any setting. Most studies recruited community volunteers. Countries: The studies were conducted in a number of countries including USA (41), Canada (4), Spain (4), Germany (4), France (2), Norway, Northern Ireland, China, Turkey, Australia, Hong Kong, Switzerland, Brazil, Denmark (2), Greece, Jamaica Settings: any included (including worksites); antenatal care settings were excluded.
Intervention(s)	**Intervention** Smoking cessation group therapy programmes
	Comparators Self-help programmes, no intervention; individual counselling; other interventions (physician/nurse advice, health education); plus NRT and NRT alone; and between programmes.
Outcomes and methods of analysis	**Outcomes** Abstinence (at least six months after start of treatment). The most rigorous definition of abstinence was used in each trial, and biochemically validated rates where available. Subjects lost to follow up were analysed as continuing smokers.
	Methods of analysis

	Effects were expressed as a relative risk for cessation. Where possible, meta-analysis was performed using a fixed-effect (Mantel-Haenszel) model. Statistical heterogeneity was calculated using I^2, values over 50% can be regarded as moderate heterogeneity and values over 75% as high.
Results	**Conclusions from systematic review** • There is reasonable evidence that groups are better than self-help, and other less intensive interventions, in helping people stop smoking, although they may be no better than advice from a healthcare provider. There is not enough evidence to determine how effective they are in comparison to intensive individual counselling. From the point of view of the consumer who is motivated to make a quit attempt it is probably worth joining a group if one is available - it will increase the likelihood of quitting. Group therapy may also be valuable as part of a comprehensive intervention which includes nicotine replacement therapy (NRT). **Findings from studies. Key comparisons:** • *Comparison of group vs self-help:* Thirteen trials compared a group programme with a self-help programme; there was an increase in cessation with the use of a group programme (N = 4375, relative risk (RR) 1.88, 95% confidence interval (CI) 1.52 to 2.33, I^2= 0%, P<0.00001). • *Comparison of group vs 'no intervention':* Nine trials with over 1000 (N= 1098) participants contributed to analysis. RR 2.60, 95% CI 1.80 to 3.76, . Heterogeneity was moderate to high (I^2 = 55%) and the estimate size is unreliable. Eight trials had higher quit rates with group programmes compared to a no-intervention or a minimal contact control, but the two highly weighted studies had amongst the smallest effects. • *Comparison of group vs individual format:* The six trials in this comparison included 980 participants. The quit rate in the controls getting individual counselling was typically between 10 and 26%, but one trial had no quitters in either arm. A pooled estimate did not detect evidence of a significant difference (RR 0.99; 95% CI 0.76 to 1.28, I^2= 9%, p=0.58). • *Comparison of group vs 'physician or nurse':* Fourteen trials with 7,286 participants contributed to this comparison. Quit rates in the advice control were typically 9 to 16% with 3 trials reporting quit rates >3% in the advice control groups.. There was statistical heterogeneity between the results (I^2 =59. There was a small benefit of group support over brief support (RR 1.22 95% CI 1.03 to 1.43). Two trials only found a statistically significant superiority of a group programme compared to advice from a healthcare provider and a pamphlet. Of the trials that did not detect significant effects three had point estimates favouring the control condition.
Limitations	**Identified by authors** • Non-participation was often high across the studies • There may be variation by the group in which they were treated, due to aspects of the group process. This aspect is generally ignored in trial analyses.

	• There is limited evidence from which to identify elements of group therapy which are most important for success.
	Identified by developers • There was limited reporting of study characteristics and link between outcomes and study quality. • Levels of intensity could be reported to clarify intervention.
Additional comments	**Comments** • Only 1 UK study was included (Northern Ireland). The majority of studies (41/66) were from USA. **Relevance to Recommendations:** • Groups may be offered as an option in addition to individual behavioural support. • Some of the studies (4) were conducted in workplace settings - which is out of scope for the guideline. • It may be difficult to attract smokers to intensive group programmes.
	Source of funding Department of Primary Health Care, Oxford University, UK. National Institute for Health Research (NIHR) School for Primary Care Research, UK.

D.4 Pharmacotherapy alone

Evidence table: Hughes et al, 2014

Bibliographic reference	Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database of Systematic Reviews* 2014, Issue 1. Art. No.: CD000031. DOI: 10.1002/14651858.CD000031.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To aim of the review is to assess the effect and safety of antidepressant medications to aid long-term smoking cessation. (Only results for bupropion are reported from this review).
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group Specialised Register which includes reports of trials indexed in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO Citation lists, recent reviews of non-nicotine pharmacotherapy, and abstracts from meetings of the Society for Research on Nicotine and Tobacco.
	Dates: July 2009– July 2013 (this is an update)
	Inclusion/exclusion criteria Included: • For efficacy: randomised trials • For safety, data from RCTs comparing antidepressant with placebo or no pharmacotherapy controls; observational data • Irrespective of publication status and language of publication. Excluded: • Trials with less than six months follow-up.

	• Trials in which all participants received the same pharmacotherapy regimen but different behavioural support
	Quality assessment: Risk of bias assessed for selection, performance and detection bias (present or absence of blinding of participants or personnel) and attrition bias (levels and reporting of loss to follow-up) and any other bias. The review reported what was considered a high or low risk of bias for performance, detection and attrition bias. An overall assessment of quality of the evidence assessed using GRADE was reported for the different comparisons. The majority of studies were judged to be at unclear risk for selection, performance and detection bias and at low risk for attrition bias. The overall quality of the evidence for the outcome abstinence (with follow-up 6 months or longer) was low (for Bupropion and NRT vs NRT alone), moderate (Bupropion vs NRT) and high (Bupropion vs placebo/control).
	Number of studies: 90 (65 for bupropion only)
Review population and setting	**Details (demographics):** N=28,283 Current cigarette smokers, or recent quitters (for trials of relapse prevention).. 2 studies included adolescents. Special populations recruited included smokers with cardiovascular disease , at risk or with COPD, with cancer, suspected tuberculosis, alcoholism, schizophrenia and post traumatic stress disorder. Most of the included studies excluded smokers with current depression but included smokers with a past history of depression.
	Setting: Countries:.North America (n=46) , multi country studies (n=3), Canada (n=2) and 1 study in the remaining countries (UK,France, Denmark, Germany, Italy, Poland, Greece, Netherlands, Australia, New Zealand, Brazil, Israel, Turkey, Pakistan). Settings: Studies were conducted in variety of settings. Clinical trial setting (n=11), clinics (n=10), cessation clinics (n=8), hospitals (n=5), outpatient (n=3), community (n=3), primary care clinics (n=3), mental health centres (n=3), multi centre (n=3), medical centres (n=4), substance misuse, preoperative clinic or health centres (n=4), educational institution (n=2). Setting was not reported or unclear in 5 studies.
Intervention(s)	**Intervention:** • Antidepressant medication
	Comparators: • Placebo or an alternative pharmacotherapy for smoking cessation • Different doses to prevent relapse or re-initiate smoking cessation
Outcomes and methods of analysis	**Outcomes:** • Efficacy was measured via a) abstinence from smoking or b) incidence of reducing cigarette consumption to 50% or less of baseline, both assessed at follow-up at least six months from start of treatment. • Safety was assessed by incidence of serious and other adverse events, and drop-outs due to adverse events.
	Methods of analysis:

	sults for abstinence for smoking expressed as risk ratio (RR). Meta-analysis using a Mantel-Haenszel fixed-effect method to estimate a pooled risk ratio with 95% confidence intervals. Where studies contributed more than one intervention arm to a pooled analysis, the control arm was split to avoid double counting. ls testing an antidepressant as a single pharmacotherapy and those testing an antidepressant as an adjunct to NRT for initial cessation were considered separately. Cessation trials and those where the intervention addressed relapse prevention or reduction in number of cigarettes smoked were considered separately. Subgroup analyses were undertaken by length of follow-up, recruitment method (clinical/community), and level of behavioural support.
Results	**Conclusions from systematic review** • There is high quality evidence to show bupropion aids long-term smoking cessation. Evidence suggests that the mode of action of bupropion is independent of the antidepressant effect and that it is of similar efficacy to nicotine replacement. Meta-analyses did not detect a significant increase in the rate of serious adverse events amongst participants taking bupropion, though the confidence interval only narrowly missed statistical significance. **Findings from studies.** **Key comparisons:** o *Comparison: bupropion vs placebo/control* There was high quality evidence that when used as the sole pharmacotherapy, bupropion significantly increased long-term cessation : 44 trials, N = 13,728; RR 1.62, 95% CI 1.49 to 1.76 , p<0.00001,I^2=18% ▪ *Subgroup by length of follow up*: There was no substantial difference in abstinence in relation to length of follow-up (12 months vs 6 months). ➢ 27 trials, n=9866; RR 1.59 95% CI 1.44 to 1.76, p<0.00001, I^2=39%; 12 month follow-up ➢ 17 trials, n=2862; RR 1.69 95% CI 1.49 to 1.97, p<0.00001, I^2=18%; 6 month follow-up o *Subgroup by level of behavioural support:* abstinence at follow up at 6 months or longer ▪ Multi session group behavioural support :10 trials, n=2001;RR 1.76 95% CI 1.44 to 2.16;p<0.00001, I^2=36% ▪ Multisession individual counselling approach : 30 trials, n= 10,964; RR 1.60 95% CI 1.46 to 1.76;p<0.00001, I^2=19% ▪ Low intensity support: 1 trial, n=47 RR 2.88 95% CI 0.32 to 25.68, p=0.34 o *Subgroup by clinical /recruitment setting:* abstinence at follow up at 6 months or longer ▪ Community volunteers: 21 trials, n= 7524; RR 1.67 95% CI 1.49 to 1.87, p<0.00001, I^2=0%

	▪ People recruited from health care settings: 18 trials, n= 3928; RR 1.60 95% CI 1.38 to 1.86, p<0.00001, I^2=20% ▪ Community + health care Settings: 1 trial, n= 540; RR 1.33 95% CI 0.83 to 2.13, p=0.23 ▪ Health care professionals/ hospital staff: 2 trials; n= 1002; RR 1.32 95% CI 0.98 to 1.78, p=0.067, I^2=79% ▪ People with a previously unsuccessful quit attempt using bupropion: 2 trials n=734; RR 2.25 95% CI 1.29 to 3.90, p=0.0041, I^2=61% o *Serious adverse events:* 33 trials, n = 9631, RR 1.30, 95% CI 1.00 to 1.69, p=0.05, I^2=0%; ▪ Subgroup analysis of cardiovascular events detected no difference between the two groups 25 trials, n=not reported; RR of 1.16 (95% CI 0.65 to 2.06, 25). ▪ Risk of about 1 in 1000 seizures associated with bupropion use. Bupropion has been associated with suicide risk but whether this is causal is unclear. • *Comparison*: *Bupropion vs NRT* :8 trials, n = 4086, RR 0.96, 95% CI 0.85 to 1.09, p=0.51, I^2=27%; 6 months or longer follow-up ▪ Patch : 6 trials, n= 1634; RR 1.04 95% CI 0.84 to 1.27, p=0.738, I^2=48% ▪ Lozenge: 2 trials, n= 694; RR 0.91 95% CI 0.67 to 1.22, p=0.51, I^2=0% ▪ Patch + lozenge: 2 trials, n= 720; RR 0.74 95% CI 0.55 to 0.98, p=0.033, I^2=0% ▪ Choice of NRT: 2 trials, n= 1038; RR 1.08, 95% CI 0.87 to 1.33, p=0.50, I^2=0% • Gender/age: Gender does not appear to consistently influence the efficacy of bupropion. Subgroup analyses of 2 trials found a larger treatment effect for older smokers and 1 study in adolescents did not show evidence of an effect for bupropion over nicotine patch alone.
Limitations	**Identified by authors** • The definition of abstinence was not always explicit and biochemical validation of self-reported smoking status was not always used. However, all but four of the bupropion studies used biochemical verification for most self-reported quitters at some assessment points.
	Identified by developers • There was limited reporting of summary study characteristics
Additional comments	**Comments** • Applicability to guideline: o Two studies included adolescents; in one study the participants were recruited from schools (setting excluded in protocol). o Setting included mental health clinics, in patient units (excluded from scope)

	○ 1 study was evaluating the effectiveness of bupropion for harm reduction (harm reduction is considered in PH45) ○ Seven studies were testing the effectiveness of bupropion for relapse prevention • 1 UK study included set in smoking cessation clinic. • For the subgroup analysis based on level of additional support, the following criteria applied in the Cochrane NRT review (Stead 2012) was applied: low intensity support was regarded as part of the provision of routine care, so the duration of time spent with the smoker (including assessment for the trial) had to be less than 30 minutes at the initial consultation, with no more than two further assessment and reinforcement visits • 26 studies had only 6 months follow-up • Of 51 bupropion studies excluded , 23 were excluded because of 'short follow-up' (duration not always reported). • Duration of pharmacotherapy before target quit data varied. **Relevance to Recommendations:** • The evidence relates to recommendation 4 in PH10. • The review includes only 1 UK study published in 2013. Seventeen additional bupropion studies were included in this update and some of the remaining included studies may have been included in PH10 development. • The review indicates that there is high quality evidence from 12 trials that bupropion for smoking cessation (compared to placebo/control) increases the likelihood of a quit attempt being successful after at least 6 months. There is moderate quality evidence to show bupropion appears to be equally effective to NRT, based on evidence from 3 trials. There is low quality evidence from 12 trials (with substantial inconsistency) showing no evidence of significant effect of adding bupropion to NRT provides an additional long-term benefit. The authors note that the serious adverse events profile for bupropion remains inconclusive.
	Source of funding Sources of internal and external support: • Department of Primary Health Care, Oxford University, UK. • Editorial base for the Cochrane Tobacco Addiction Group • National Institute for Health Research School for Primary Care Research, UK. • Support for the Department of Primary Health Care, Oxford University • National Institute on Drug Abuse (NIDA), USA • NHS Research and Development Programme.UK

Evidence table: Stead et al, 2012 (NRT)

Bibliographic reference	Stead LF, Perera R, Bullen C,Mant D, Hartmann-Boyce J, Cahill K, Lancaster T. Nicotine replacement therapy for smoking cessation. *Cochrane Database of*

	Systematic Reviews 2012, Issue 11. Art. No.: CD000146. DOI: 10.1002/14651858.CD000146.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To aims of the review were: • To determine the effect of NRT compared to placebo in aiding smoking cessation, and to consider whether there is a difference in effect for the different forms of NRT (chewing gum, transdermal patches, oral and nasal sprays, inhalers and tablets/lozenges) in achieving abstinence from cigarettes. • To determine whether the effect is influenced by the dosage, form and timing of use of NRT; the intensity of additional advice and support offered to the smoker; or the clinical setting in which the smoker is recruited and treated. • To determine whether combinations of NRT are more likely to lead to successful quitting than one type alone. • To determine whether NRT is more or less likely to lead to successful quitting compared to other pharmacotherapies.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Register :CENTRAL, MEDLINE, EMBASE, PsycINFO • Handsearching of abstract books from meetings of the Society for Research on Nicotine & Tobacco • Search methods employed in earlier updates that did not result in any additional trials were not utilised for this update.
	Dates: December 1996-July 2012
	Inclusion/exclusion criteria Included: • Randomised trials (unit of randomisation was therapists rather than smokers); trials where allocation to treatment was by a quasi-randomised method • Men or women who smoked and were motivated to quit irrespective of setting from which they were recruited and/or their initial level of nicotine dependence. Excluded: • Trials which did not report cessation rates or • Trials with follow-up of less than 6 months (except for trials amongst pregnant women) • Trials that evaluated the number of cigarettes smoked rather than to quit (NB:harm reduction approaches were included in the original review and are now covered in a separate Cochrane review)
	Quality assessment: Risk of bias for each study assessed on five domains: selection bias (random sequence generation; allocation concealment), performance and detection bias (blinding), and attrition bias (levels and reporting of loss to follow-up). Overall quality of the evidence for an outcome was assessed using GRADE. Most studies were considered to be low or unclear risk of bias.
	Number of studies: 150 trials (18 new studies included in the update)
Review population and setting	**Details (demographics):** The median sample size was around 240 but ranged from fewer than 50 to over 3500 participants.

	Participants were typical adult cigarette smokers with an average age of 40 to 50. Some trials included light smokers. Most trials had similar numbers of men and women.
	Setting: Countries: Trials were conducted in North America (n=77 studies), Europe (n=60 including 18 UK studies), Australasia (n=5), Japan (n=2 studies), South America (n=2), and 1 study each in South Africa, Taiwan, Thailand, and in multiple regions. Settings: Community (treatment provided in medical setting) (n=66), primary care (n=23), smoking cessation clinics (n=10), hospital in or outpatients (n=10), setting intended to resemble 'over the counter' use of NRT (n=6), antenatal clinics (n=4), workplace (n=4), university clinic (n=1), national quit line (n=1). The remaining trials were undertaken in participants from the community, most of whom had volunteered in response to media advertisements, but who were treated in clinical settings.
Intervention(s)	**Intervention:** • NRT (including chewing gum, transdermal patches, nasal and oral spray, inhalers and tablets or lozenges) • NRT with additional support (low or high intensity). Support that could be offered as part of routine medical care was considered 'low intensity'. Where level of support exceeded 30 minutes, support was categorised as high.
	Comparators: • Placebo • No NRT control
Outcomes and methods of analysis	**Outcomes:** • Abstinence from smoking after at least 6 month of follow-up (where possible, measures of sustained cessation rather than point prevalence were chosen)
	Methods of analysis: Risk ratios were calculated and where appropriate meta-analysis using a Mantel-Haenszel fixed-effect model with 95% confidence intervals. I^2 greater than 50% was considered to indicate substantial heterogeneity. Meta-regression was used to test for significant where estimates of effect differed across subgroups**.** People who dropped out or were lost to follow-up were regarded as continuing smokers.
Results	**Conclusions from systematic 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. NRTs increase the rate of quitting by 50 to 70%, regardless of setting. The effectiveness of NRT appears to be largely independent of the intensity of additional support provided to the individual. Provision of more intense levels of support, although beneficial in facilitating the likelihood of quitting, is not essential to the success of NRT. **Findings from studies. Key comparisons:**

	Outcome: Smoking cessation
	• *Comparison NRT (any form) vs control*: 117 trials, n=51,265; RR 1.60 95% CI 1.53 to 1.68; I^2=30%; p<0.00001;follow-up 6-24 months
	• *Comparison Nicotine gum vs control:* 56 trials, n=22,581 RR 1.49 95% CI 1.40 to 1.60; p<0.00001, I^2=40%
	• *Comparison Nicotine gum vs control Subgroup analysis level of behaviour support:* 55 trials, n=21.759 RR 1.50 95% CI 1.40 to 1.61; p<0.00001, I^2=41%
	  ○ Low intensity support 17 trials ,n=11,257; RR 1.66 95% CI 1.46 to 1.88, p<0.00001, I^2=62%
	  ○ High intensity individual support 18 trials, n= 6891; RR 1.32 95% CI 1.18 to 1.49, p<0.00001, I^2=2%
	  ○ High intensity group-based support 20 trials, n= 3611 RR 1.57 95% CI 1.40 to 1.76, p<0.00001, I^2=25%
	• *Comparison Nicotine patch vs control:* 43 trials, n=19,586; RR 1.64 95% CI 1.52 to 1.78, p< 0.0001, I^2=19%
	• *Comparison Nicotine patch vs control: Subgroup analysis level of behaviour support* 43 trials, n=19,585; RR 1.64 95% CI 1.52 to 1.78, p< 0.0001, I^2=16%
	  ○ Low intensity support 12 trials, n= 4388; RR 1.78 95% CI 1.49 to 2.12, p< 0.0001, I^2=0%
	  ○ High intensity individual support 22 trials; n=11,559 RR 1.59 95% CI 1.41 to 1.78, p<0.00001, I^2=42%
	  ○ High intensity group-based support 10 trials, n=3638; RR 1.65 95% CI 1.43 to 1.90, p< 0.0001, I^2=0%
	• Comparison *Oral tablets/lozenges vs control* : 6 trials, n=3,405; RR 1.95 95% 1.61 to 2.36, p<0.00001, I^2=24%
	• *Comparison Nicotine inhaler vs control:* 4 trials, n=976; RR 1.90 95% CI 1.36 to 2.67, p< 0.0001, I^2=0%
	• *Comparison Nicotine nasal spray vs control:* 4 trials, n=887; RR 2.02 95% CI 1.49 to 2.73, p< 0.0001, I^2=0%
	• *Comparison Oral spray vs control:* 1 trial, n=479; RR 2.48 95% CI 1.24 to 4.94, p=0.010
	• *Comparison Nicotine patch and inhaler vs control*: 1 trial, n=245; RR 1.07 95% CI 0.57 to 1.99, p=0.83
	• *Comparison Nicotine patch and lozenge vs control*: 1 trial, n=308; RR 1.83 95% CI 1.01 to 3.31, p=0.048
	• *Comparison Choice of NRT product*: 5 trials, n=2798; RR 1.60 95% CI 1.39 to 1.84, p< 0.0001, I^2=0%
	• *Comparison NRT (patch; lozenge) vs bupropion*: 5 trials, n=2544; RR 1.01 95% CI 0.87 to 1.18, p=0.86, I^2=40%

	• Comparison NRT (patch; gum; lozenge) + bupropion vs bupropion: 4 trials, n=1991; RR 1.24 95 % CI 1.06 to 1.45, p=0.0066, I^2=57% • Comparison NRT (patch; lozenge) + bupropion vs bupropion: 2 trials, n=704; RR 2.61 95% CI 1.65 to 4.12, p=0.000040, I^2=76% • Level of behaviour support: Longer vs short support 3 trials, n=800 RR 1.14 95% CI 0.88 to 1.47, p=0.32, I^2=0% o *Comparison Nicotine gum vs control* Long vs short support 2 trials, n=296; RR 1.22 95% CI 0.77 to 1.92, p=0.39, I^2=0% o *Comparison Nicotine patch vs control* Long vs short support 1 trial; n=504; RR 1.10 95% CI 0.81 to 1.49, p=0.54 • Comparison NRT *(patch;inhaler) purchase without support[stimulated OTC setting] vs physician support:* 2 trials, n=820; RR 4.58 95% CI 1.18 to 17.88, p=0.28, I^2=0% • Comparison combination NRT (n=1785) versus single NRT (n=2879): 9 trials RR 1.34 [1.18, 1.51] I^2=34% • Additional subgroup analyses : (*results for these subgroup analyses are reported in the review but a narrative summary is provided here*) o Treatment setting: A subgroup analysis did not detect differences in relative effect according to the setting of recruitment and treatment. A post hoc meta-regression showed there that the type of NRT did not influence effect sizes differently in different settings. o Definition of abstinence: A subgroup analysis assessed whether sustained abstinence at 12 months had different treatment effects from those that only reported a point prevalence outcome, or had shorter follow-up. For nicotine gum a higher estimate was reported in a meta-regression for studies reporting sustained abstinence at 6 months, but this was attributed to one study. The review authors noted it is unlikely to be of methodological or clinical significance. For nicotine patch the risk ratios did not differe significantly between subgroups. Outcome: Adverse events (Palpitations/chest pains) • C*omparison NRT vs placebo* 15 trials, n=11,074; OR 1.88 95% CI 1.37 to 2.57, p=0.000084, I^2=10% The review also reports results for duration of therapy, dosage, and effect of weaning/tapering dose at end of treatment.
Limitations	**Identified by authors** • Possible methodological limitations of the review is use of data predominantly derived from published reports and publication bias. • Magnitude of effectiveness of NRT may be smaller than estimates in the review suggest. The authors based this on the funnel plot which showed some asymmetry for trials in the main comparison and based on a meta-analysis that has demonstrated that studies which received pharmaceutical funding have slightly higher effect sizes.

	Identified by developers • Limited terms used in the search strategy

Additional comments	**Comments**
	• Applicability to guideline:
	  ○ The review includes four trials which recruited only pregnant women (excluded from the scope). The results from these studies are included in the overall pooled effect reported above. The results are also presented separately in the review.
	  ○ 1 study includes adolescents
	  ○ 1 study recruited from workplace setting and 2 studies were undertaken in a workplace setting (setting excluded from scope)
	• 18 UK studies included (1 study included pregnant women).
	
	Relevance to Recommendations:
	• The evidence relates to 4 in PH10.
	• In majority of the studies recruitment was from the community (with treatment provided in medical setting).
	• Of the 18 new studies included, 2 included UK population. 2 studies included pregnant women (excluded from scope) of which 1 was a UK study. The studies included in the original review may have been included in PH10 development.
	• The review notes that the evidence suggests no overall difference in effectiveness between different forms of NRT, nor a benefit for using patches beyond eight weeks. NRT works with or without additional counselling. People who use NRT during a quit attempt are likely to further increase their chance of success by using a combination of the nicotine patch and a faster acting form or by combining the patch with bupropion. Data suggest that starting to use NRT patches shortly before the planned quit date may increase the chance of success. Adverse effects from using NRT are related to the type of product, and include skin irritation from patches and irritation to the inside of the mouth from gum and tablets. There is no evidence of effect to suggest that NRT increases the risk of heart attacks.

	Source of funding Internal sources: • Department of Primary Health Care, Oxford University, UK. • Editorial base for the Cochrane Tobacco Addiction Group • National Institute for Health Research School for Primary Care Research, UK. • Support for the Department of Primary Health Care, Oxford University External sources: • NHS Research and Development Programme, UK. • Infrastructure funding for the Cochrane Tobacco Addiction Group

D.5 Pharmacotherapy with behavioural support

Evidence table: Hughes et al, 2014

Bibliographic reference	Hughes JR, Stead LF, Hartmann-Boyce J, Cahill K, Lancaster T. Antidepressants for smoking cessation. *Cochrane Database of Systematic Reviews* 2014, Issue 1. Art. No.: CD000031. DOI: 10.1002/14651858.CD000031.pub4.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To aim of the review is to assess the effect and safety of antidepressant medications to aid long-term smoking cessation. (Only results for bupropion are reported from this review).
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group Specialised Register which includes reports of trials indexed in the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO Citation lists, recent reviews of non-nicotine pharmacotherapy, and abstracts from meetings of the Society for Research on Nicotine and Tobacco.
	Dates: July 2009– July 2013 (this is an update)
	Inclusion/exclusion criteria Included: • For efficacy: randomised trials • For safety, data from RCTs comparing antidepressant with placebo or no pharmacotherapy controls; observational data • Irrespective of publication status and language of publication. Excluded: • Trials with less than six months follow-up. • Trials in which all participants received the same pharmacotherapy regimen but different behavioural support
	Quality assessment: Risk of bias assessed for selection, performance and detection bias (present or absence of blinding of participants or personnel) and attrition bias (levels and reporting of loss to follow-up) and any other bias. The review reported what was considered a high or low risk of bias for performance, detection and attrition bias. An overall assessment of quality of the evidence assessed using GRADE was reported for the different comparisons. The majority of studies were judged to be at unclear risk for selection, performance and detection bias and at low risk for attrition bias. The overall quality of the evidence for the outcome abstinence (with follow-up 6 months or longer) was low (for Bupropion and NRT vs NRT alone), moderate (Bupropion vs NRT) and high (Bupropion vs placebo/control).
	Number of studies: 90 (65 for bupropion only)
Review population and setting	**Details (demographics):** N=28,283 Current cigarette smokers, or recent quitters (for trials of relapse prevention).. 2 studies included adolescents. Special populations recruited included smokers with cardiovascular disease , at risk or with COPD, with cancer, suspected tuberculosis, alcoholism, schizophrenia and post traumatic stress disorder. Most of the included studies excluded smokers with current depression but included smokers with a past history of depression.
	Setting: Countries:.North America (n=46) , multi country studies (n=3), Canada (n=2) and 1 study in the remaining countries (UK,France, Denmark, Germany, Italy,

	Poland, Greece, Netherlands, Australia, New Zealand, Brazil, Israel, Turkey, Pakistan). Settings: Studies were conducted in variety of settings. Clinical trial setting (n=11), clinics (n=10), cessation clinics (n=8), hospitals (n=5), outpatient (n=3), community (n=3), primary care clinics (n=3), mental health centres (n=3), multi centre (n=3), medical centres (n=4), substance misuse, preoperative clinic or health centres (n=4), educational institution (n=2). Setting was not reported or unclear in 5 studies.
Intervention(s)	**Intervention:** • Antidepressant medication
	Comparators: • Placebo or an alternative pharmacotherapy for smoking cessation • Different doses to prevent relapse or re-initiate smoking cessation
Outcomes and methods of analysis	**Outcomes:** • Efficacy was measured via a) abstinence from smoking or b) incidence of reducing cigarette consumption to 50% or less of baseline, both assessed at follow-up at least six months from start of treatment. • Safety was assessed by incidence of serious and other adverse events, and drop-outs due to adverse events.
	Methods of analysis: Results for abstinence for smoking expressed as risk ratio (RR). Meta-analysis using a Mantel-Haenszel fixed-effect method to estimate a pooled risk ratio with 95% confidence intervals. Where studies contributed more than one intervention arm to a pooled analysis, the control arm was split to avoid double counting. Trials testing an antidepressant as a single pharmacotherapy and those testing an antidepressant as an adjunct to NRT for initial cessation were considered separately. Cessation trials and those where the intervention addressed relapse prevention or reduction in number of cigarettes smoked were considered separately. Subgroup analyses were undertaken by length of follow-up, recruitment method (clinical/community), and level of behavioural support.
Results	**Conclusions from systematic review** • There is high quality evidence to show bupropion aids long-term smoking cessation. Evidence suggests that the mode of action of bupropion is independent of the antidepressant effect and that it is of similar efficacy to nicotine replacement. Meta-analyses did not detect a significant increase in the rate of serious adverse events amongst participants taking bupropion, though the confidence interval only narrowly missed statistical significance. **Findings from studies.** **Key comparisons:** ○ *Comparison: bupropion vs placebo/control* There was high quality evidence that when used as the sole pharmacotherapy, bupropion significantly increased long-term cessation : 44 trials, N = 13,728; RR 1.62, 95% CI 1.49 to 1.76 , p<0.00001,I^2=18%

- *Subgroup by length of follow up*: There was no substantial difference in abstinence in relation to length of follow-up (12 months vs 6 months).
  - 27 trials, n=9866; RR 1.59 95% CI 1.44 to 1.76, p<0.00001, I^2=39%; 12 month follow-up
  - 17 trials, n=2862; RR 1.69 95% CI 1.49 to 1.97, p<0.00001, I^2=18%; 6 month follow-up

- *Subgroup by level of behavioural support:* abstinence at follow up at 6 months or longer
  - Multi session group behavioural support :10 trials, n=2001;RR 1.76 95% CI 1.44 to 2.16;p<0.00001, I^2=36%
  - Multisession individual counselling approach : 30 trials, n= 10,964; RR 1.60 95% CI 1.46 to 1.76;p<0.00001, I^2=19%
  - Low intensity support: 1 trial, n=47 RR 2.88 95% CI 0.32 to 25.68, p=0.34

- *Subgroup by clinical /recruitment setting:* abstinence at follow up at 6 months or longer
  - Community volunteers: 21 trials, n= 7524; RR 1.67 95% CI 1.49 to 1.87, p<0.00001, I^2=0%
  - People recruited from health care settings: 18 trials, n= 3928; RR 1.60 95% CI 1.38 to 1.86, p<0.00001, I^2=20%
  - Community + health care Settings: 1 trial, n= 540; RR 1.33 95% CI 0.83 to 2.13, p=0.23
  - Health care professionals/ hospital staff: 2 trials; n= 1002; RR 1.32 95% CI 0.98 to 1.78, p=0.067, I^2=79%
  - People with a previously unsuccessful quit attempt using bupropion: 2 trials n=734; RR 2.25 95% CI 1.29 to 3.90, p=0.0041, I^2=61%

- *Serious adverse events:* 33 trials, n = 9631, RR 1.30, 95% CI 1.00 to 1.69, p=0.05, I^2=0%;
  - Subgroup analysis of cardiovascular events detected no difference between the two groups 25 trials, n=not reported; RR of 1.16 (95% CI 0.65 to 2.06, 25).
  - Risk of about 1 in 1000 seizures associated with bupropion use. Bupropion has been associated with suicide risk but whether this is causal is unclear.

- *Comparison*: *Bupropion vs NRT* :8 trials, n = 4086, RR 0.96, 95% CI 0.85 to 1.09, p=0.51, I^2=27%; 6 months or longer follow-up
  - Patch : 6 trials, n= 1634; RR 1.04 95% CI 0.84 to 1.27, p=0.738, I^2=48%
  - Lozenge: 2 trials, n= 694; RR 0.91 95% CI 0.67 to 1.22, p=0.51, I^2=0%
  - Patch + lozenge: 2 trials, n= 720; RR 0.74 95% CI 0.55 to 0.98, p=0.033, I^2=0%
  - Choice of NRT: 2 trials, n= 1038; RR 1.08, 95% CI 0.87 to 1.33, p=0.50, I^2=0%

- Gender/age: Gender does not appear to consistently influence the efficacy of bupropion. Subgroup analyses of 2 trials found a larger

	treatment effect for older smokers and 1 study in adolescents did not show evidence of an effect for bupropion over nicotine patch alone.
Limitations	**Identified by authors** • The definition of abstinence was not always explicit and biochemical validation of self-reported smoking status was not always used. However, all but four of the bupropion studies used biochemical verification for most self-reported quitters at some assessment points.
	Identified by developers • There was limited reporting of summary study characteristics
Additional comments	**Comments** • Applicability to guideline: o Two studies included adolescents; in one study the participants were recruited from schools (setting excluded in protocol). o Setting included mental health clinics, in patient units (excluded from scope) o 1 study was evaluating the effectiveness of bupropion for harm reduction (harm reduction is considered in PH45) o Seven studies were testing the effectiveness of bupropion for relapse prevention • 1 UK study included set in smoking cessation clinic. • For the subgroup analysis based on level of additional support, the following criteria applied in the Cochrane NRT review (Stead 2012) was applied: low intensity support was regarded as part of the provision of routine care, so the duration of time spent with the smoker (including assessment for the trial) had to be less than 30 minutes at the initial consultation, with no more than two further assessment and reinforcement visits • 26 studies had only 6 months follow-up • Of 51 bupropion studies excluded , 23 were excluded because of 'short follow-up' (duration not always reported). • Duration of pharmacotherapy before target quit data varied. **Relevance to Recommendations:** • The evidence relates to recommendation 4 in PH10. • The review includes only 1 UK study published in 2013. Seventeen additional bupropion studies were included in this update and some of the remaining included studies may have been included in PH10 development. • The review indicates that there is high quality evidence from 12 trials that bupropion for smoking cessation (compared to placebo/control) increases the likelihood of a quit attempt being successful after at least 6 months. There is moderate quality evidence to show bupropion appears to be equally effective to NRT, based on evidence from 3 trials. There is low quality evidence from 12 trials (with substantial inconsistency) showing no evidence of significant effect of adding bupropion to NRT provides an additional long-term benefit. The authors note that the serious adverse events profile for bupropion remains inconclusive.
	Source of funding Sources of internal and external support: • Department of Primary Health Care, Oxford University, UK. • Editorial base for the Cochrane Tobacco Addiction Group • National Institute for Health Research School for Primary Care Research, UK.

	• Support for the Department of Primary Health Care, Oxford University • National Institute on Drug Abuse (NIDA), USA • NHS Research and Development Programme.UK

Evidence table: Lancaster & Stead, 2017(Individual counselling)

Bibliographic reference	Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews2017, Issue 3. Art. No.: CD001292. DOI: 10.1002/14651858.CD001292.pub3.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To determine the effects of individual counselling.
Review quality	+
Review search parameters	**Sources** • Cochrane Tobacco Addiction Group Specialized Register. Previous reviews and meta-analyses, including all studies in the previous US guidelines.
	Dates: -May 2016
	Inclusion/exclusion criteria Included: • RCTs and quasi-RCTs. • Cessation assessed at 6 months after start of intervention.(minimum follow up of 6 months) • One treatment arm consisted of an unconfounded intervention from a counsellor. Excluded: • Trials recruiting only pregnant women • Trials recruiting only children and adolescents. • Counselling delivered by doctors and nurses as part of clinical care • Interventions which address multiple risk factors in addition to smoking.
	Quality assessment: Risk of bias assessment included: four domains of study quality; randomisation sequence generation; sequence concealment, blinding during treatment and follow up; and incomplete outcome data.
	Number of studies: 49.
Review population and setting	**Details (demographics):** Over 19000 participants. Any smokers (except pregnant women). A common setting for delivery of advice was secondary care, therefore many of the participants were hospital in- or outpatients.
	Setting: Countries: The vast majority of studies were conducted in USA (30 of 49). Other countries included UK (2), Denmark (3), Spain (3), Australia (2), Germany, Switzerland, Sweden, Hong Kong, ChinaS. Korea, Japan, Netherlands and India. Settings: 19 of 49 studies recruited in in-patient settings (out of scope). Other studies recruited a mixture of primary and community settings. 2 studies recruited only women.
Intervention(s)	**Intervention:** • Individual counselling as a face-to-face encounter between a smoking patient and a counsellor trained in assisting smoking cessation.
	Comparators: • No advice (or usual care) or less intensive counselling interventions.

	• Individual counselling versus no treatment, brief advice or self-help materials • More intensive versus less intensive individual counselling • Comparisons between counselling methods matched for contact time.
Outcomes and methods of analysis	**Outcomes:** • Abstinence (at least six months after start of treatment); used sustained abstinence, or multiple prevalence where available. • The most rigorous definition of abstinence was used in each trial. • With or without biochemically validated rates. • Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis, where appropriate. Individual study results summarised as a risk ratio. Where appropriate a Mantel-Haenszel fixed effect method to estimate a pooled risk ration with 95% CI.
Results	**Conclusions from systematic review** • The review looked at trials of counselling by a trained therapist providing one or more face-to-face sessions, separate from medical care. All the trials involved sessions of more than 10 minutes, with most also including further telephone contact for support. The review found that individual counselling could help smokers quit, but there was not enough evidence about whether more intensive counselling was better. **Findings from studies. Key comparisons:** • *Comparison individual counselling vs minimal contact (usual care to up to 10 minutes of advice).* Thirty-three trials compared individual counselling to a minimal behavioural intervention. Individual counselling was more effective than control. The relative risk (RR) for smoking cessation at long-term follow up was 1.48, 95% confidence interval (CI) 1.34 to 1.64, p<0.00001. I^2=46% N = 13762 participants. • *Comparison individual counselling vs control (no systematic pharmacotherapy).* The subgroup of twenty-seven trials compared individual counselling to a control group (without pharmacotherapy). Individual counselling was more effective than control. The relative risk (RR) for smoking cessation at a long-term follow up was 1.57, 95% confidence interval (CI) 1.40 to 1.77, p<0.00001, I^2= 50% N = 11100 partcipants. • *Comparison: Counselling plus pharmacotherapy vs pharmacotherapy alone*. N= 2662, 6 trials. The subgroup of six studies where counselling was tested as an adjunct to nicotine replacement therapy or bupropion had a smaller estimated effect which just reached significance (RR 1.24; 95% CI 1.01 to 1.51).I^2=0%, p=0.04. • *Comparison more intensive counselling vs brief counselling.* In an analysis combining eleven studies, there was some evidence of

	benefit from more intensive compared to brief counselling (RR 1.29; 95% CI 1.09 to 1.53). n=2920 I^2= 48%. • *Comparison more intensive counselling vs brief counselling (no pharmacotherapy)* The subgroup of four trials compared more intensive counselling with brief counselling without pharmacotherapy and found no difference between the groups. RR 1.42 95% CI 0.98 to 2.06, N = 872 • *Comparison more intensive counselling vs brief counselling (adjunct to pharmacotherapy).* The subgroups analysis of 8 trials found some benefit with more intensive counselling compared to brief counselling when adjunct to pharmacotherapy. RR 1.26 95% CI 1.04 to 1.52, N = 2048
Limitations	**Identified by authors** • The review was not able to identify the most effective intensity and duration of intervention for different populations.
	Identified by developers • Overall, description of methods and analysis was limited.
Additional comments	**Comments** • Lack of interest in quitting was not an explicit exclusion criteria in any study, but the level of motivation to quit smoking was sometimes difficult to assess. **Relevance to Recommendations:** • Various studies included secondary care patients and (to a lesser degree) worksites. It is not clear whether lower intensity (even brief advice) is more or less effective in primary and community settings from this evidence. The authors do state 'Almost half the trials recruited people in hospital settings, but there was no evidence of heterogeneity of results in different settings'. • The review included only 2 UK studies. • The review indicates that intensive counselling (more than 10 minutes) is more effective than brief advice.
	Source of funding Internal Oxford University Department of Primary Health Care, UK. National Institute for Health Research School for Primary Care Research, UK. External NHS Research and Development Programme, UK.

Evidence table: Mdege et al 2014

Bibliographic reference	Mdege N D, and Chindove S. 2014. "Effectiveness of tobacco use cessation interventions delivered by pharmacy personnel: A systematic review". Research in Social & Administrative Pharmacy 10:21-44.
Review design	Systematic Review (narrative summary)

Aim of review	This review aimed to identify, describe and synthesis currently available evidence on the effectiveness of tobacco use cessation interventions delivered by pharmacy personnel.
Review quality	+
Review search parameters	**Sources** • MEDLINE, EMBASE, PSYCINFO, Cochrane Library, Web of Knowledge and the Current Controlled Trials Register.
	Dates: up until May 2012
	Inclusion/exclusion criteria Included: • Controlled clinical trials (CCTs), cluster randomised controlled trials (CCRTs) and randomized controlled trials (RCTs), which were comparing any pharmacy personnel delivered tobacco use cessation intervention to no treatment, usual care or other active treatments Excluded: •
	Quality assessment: Study quality assessment included adequacy of sequence generation and allocation concealment, sample size/power calculation, blinding, handling of incomplete data, follow-up rates, use of intention to treat.
	Number of studies: 10
Review population and setting	**Details (demographics):** N=20,133
	Setting: *Awaiting retrieval of supplementary material prior to presenting these findings* Countries: 3 for UK and USA, and 1 each for Canada, Denmark, Japan and Australia. Settings:
Intervention(s)	**Intervention:**
	Comparators: Usual care
Outcomes and methods of analysis	**Outcomes:** Abstinence (e.g., point prevalence; continuous abstinence) and relapse (e.g., time to relapse) as measured by the respective studies.
	Methods of analysis: Narrative summary
Results	**Conclusions from systematic review** *Awaiting retrieval of supplementary material prior to presenting these findings* **Findings from studies** *Awaiting retrieval of supplementary material prior to presenting these findings*
Limitations	**Identified by authors**

	Identified by developers •
Additional comments	**Comments** **Relevance to Recommendations:** •
	Source of funding Internal sources: •

Evidence table: Stead & Lancaster, 2016(Combined therapy)

Bibliographic reference	Stead LF, Koilpillai P, Fanshawe TR, Lancaster T. Combined pharmacotherapy and behavioural interventions for smoking cessation. Cochrane Database of Systematic Reviews 2016, Issue 3. Art. No.: CD008286. DOI: 10.1002/14651858.CD008286.pub3.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To assess the effect of combining behavioural support and medication to aid smoking cessation, compared to a minimal intervention or usual care, and to identify whether there are different effects depending on characteristics of the treatment setting, intervention, population treated, or take-up of treatment.
Review quality	++
Review search parameters	**Sources** • Cochrane Tobacco Addiction Specialised Register: from regular searches of The Cochrane Library, MEDLINE, EMBASE,PsycINFO.
	Dates: -July 2015.
	Inclusion/exclusion criteria Included: • RCTs and quasi-RCTs • Any language • People who smoke - interest in quitting was not a requirement. • Any setting Excluded: • Trials recruiting only pregnant women • Trials recruiting only adolescents. • Trials with less than 6 months follow up • Trials were fewer than 20% participants were eligibile for or used pharmacotherapy.
	Quality assessment: Risk of bias assessment included: random sequence generation and allocation concealment as markers for the risk of selection bias, and assessment of the level and reporting of incomplete outcome data as a measure of attrition bias. Quality of evidence assessed using GRADE; cessation at longest follow up (all but Lung Health Study): high; cessation at longest follow follow up (Lung health Study only): moderate. People lost to follow up were assumed to be continuing smoking.

	Number of studies: 53
Review population and setting	**Details (demographics):** More than 25,000 participants. Did not need to be selected in their interest in quitting or their suitability for pharmacotherapy. Trials typically had between 35 to 65% female participants. Two trials recruited only women and one only men. Three trials in the US Veterans Administration medical system had higher proportions of men as did one trial in Spanish workplaces. The average age ranged from low 40s to mid 50s.
	Setting: Countries: About half the studies were conducted in the USA. Of the others there were four from Canada three from Australia; three from Denmark, two from Spain, two from the UK and one each from Brazil, Italy, the Netherlands (Kotz 2009), Sweden (Sadr Azodi 2009),Japan and Hong Kong. Settings: A high proportion of studies were conducted in healthcare settings (among people with specific health needs). Only six trials were in primary care settings and 2 in dental settings.
Intervention(s)	**Intervention:** • Combination behavioural support (such as brief advice and counselling) and medications (including varenicline, bupropion, and nicotine replacement therapies like patches or gum) help people quit smoking. • The typical intervention involved multiple contacts with a specialist cessation adviser or counsellor, with most participants using some pharmacotherapy and receiving multiple contacts. However, there was a great deal of variation, including some interventions which involved making pharmacotherapy and behavioural components available to a large population in which take-up of treatment was low or providing a brief intervention to all participants and offering stepped care for those willing to set a quit date. • More than half the trials (n = 22, 54%) offered between four and eight sessions and around a quarter (n = 11, 27%) over eight sessions. • Most counselling and support was provided by specialist cessation counsellors or trained trial personnel. • Intensity of the intervention was measured using planned contact time and number of sessions where possible (see pg.7 for further details).
	Comparators: • The treatment offered to the control group typically involved brief advice and self-help materials. Control group participants could be offered usual care, self-help materials or brief advice on quitting, but support had to be of lower intensity than that given to intervention participants.
Outcomes and methods of analysis	**Outcomes:** Abstinence (at least six months after start of treatment). The most rigorous definition of abstinence was used in each trial, and biochemically validated rates where available. Subjects lost to follow up were analysed as continuing smokers.
	Methods of analysis:

	For groups of trials where meta-analysis was judged appropriate, relative risks were pooled using a Mantel-Haenszel fixed-effect model, and a pooled estimate with 95% confidence intervals reported. Where trials had more than one intervention condition a comparison was made of the most intensive combination of behavioural support and pharmacotherapy to the control in the main analysis.
Results	**Conclusions from systematic review** • Interventions that combine pharmacotherapy and behavioural support increase smoking cessation success compared to a minimal intervention or usual care. Further trials would be unlikely to change this conclusion. We did not find strong evidence from indirect comparisons that offering more intensive behavioural support was associated with larger treatment effects but this could be because intensive interventions are less likely to be delivered in full. **Findings from studies. Key comparisons:** • *Comparison. One large study (the Lung Health Study) vs usual care or brief advice or less intensive behavioural support*. N= 5887. Since this study used a particularly intensive intervention which included extended availability of nicotine gum, multiple group sessions and long term maintenance and recycling contacts, the results may not be comparable with the interventions used in other studies, and hence it was not pooled in other analyses. It reported a large treatment effect (RR 3.88, 95% CI 3.35 to 4.50, I^2 not applicable, p<0.00001).GRADE quality assessment= moderate. • *Comparison: combined pharmacotherapy and behavioural interventions vs usual care or brief advice or less intensive behavioural support*. Based on 52 studies (N = 19,488 participants) there was good evidence for a benefit of combination pharmacotherapy and behavioural treatment compared to usual care or brief advice or less intensive behavioural support (RR 1.83, 95% CI 1.68 to 1.98, p<0.00001) with moderate statistical heterogeneity (I^2 = 36%). GRADE quality assessment= high. • The pooled estimate for 43 trials (n= 13,863) that recruited participants in healthcare settings (RR 1.97, 95% CI 1.79 to 2.18, I^2=39%, p<0.00001) was higher than for eight trials (n=4906) with community-based recruitment (RR 1.53, 95% CI 1.33 to 1.76, I^2=11%, p<0.00001). • Pooled estimates were lower in a subgroup of trials where the behavioural intervention was provided by specialist counsellors versus trials where counselling was linked to usual care (specialist: RR 1.81, 95% CI 1.64 to 1.99 I^2=25%, p<0.00001, 39 trials (n= 12,252); usual provider: RR 2.03, 95% CI 1.70 to 2.43 I^2= 54%,p<0.00001 , 9 trials (n=5112)) but this was largely attributable to the small effect size in two trials using specialist counsellors where the take-up of the planned intervention was low, and one usual provider trial with a large effect.
Limitations	**Identified by authors**

	• No assessment was made of risk of bias from lack of blinding. • In most of the trials intervention group participants would have known they were receiving active medications - with no placebo groups.
	Identified by developers • None
Additional comments	**Comments** • N/A **Relevance to Recommendations:** • About half the studies were conducted in the USA, with only 4 studies from UK. • 10 trials were with hospital inpatients, and additional 7 studies with secondary care patients - all out of guideline scope. • Combination pharmacotherapy and behavioural support increase smoking cessation. • Most of the trials offered one or more types of NRT, or bupropion and are relevant to the guideline. • The evidence was not clear from indirect comparisons that increasing contact (intensity) increased quit success - but there was a trend in that direction.
	Source of funding Department of Primary Care Health Sciences, University of Oxford, UK. NHS, National Institute of Health Research, UK. National School for Health Research, School for Primary Care Research, UK .

Evidence table: Stead et al, 2015

Bibliographic reference	Stead LF, Koilpillai P, Lancaster T. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No.: CD009670. DOI: 10.1002/14651858.CD009670.pub3.
Review design	Cochrane Systematic Review (with meta analysis)
Aim of review	To evaluate the effect of increasing the intensity of behavioural support for people using smoking cessation medications, and to assess whether there are different effects depending on the type of pharmacotherapy, or the amount of support in each condition.
Review quality	++
Review search parameters	**Sources** • Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO for trials of smoking cessation or prevention interventions.
	Dates: -May 2015
	Inclusion/exclusion criteria Included: • RCTs and quasi-RCTs. • Person-to-person contact • Cessation assessed at 6 months after start of intervention. Excluded: • Trials recruiting only pregnant women • Trials recruiting only young people and adolescents • Trials that used a contact-matched control to evaluate differences to evaluate differences between types or components of support.
	Quality assessment: Risk of bias assessment included: randomisation procedure, allocation concealment, incomplete outcome, data assessment and any other bias.
	Number of studies: 47.
Review population and setting	**Details (demographics):** Over 18,000 participants. .Expected to be relatively motivated and prepared to use medication as part of their quit attempt (however motivation to quit was not always an explicit eligibility criterion).
	Setting: Countries: The vast majority of studies were conducted in USA (37 of 47). Other countries included Netherlands (2), with UK, Denmark, Spain, Greece, Germany, Australia, Canada, Turkey, Brazil all with 1 study each Settings: Recruitment in any setting: fifteen studies recruited people in a healthcare setting (excluding smoking cessation clinics); this included 5 studies in primary care, 1 in a chest clinic, 1 in a cardiovascular disease outpatient clinic, 2 in HIV clinics, 1 in mental health clinics, 3 in substance abuse clinics, one in a Veterans Administration hospital, and 1 in cardiac wards.
Intervention(s)	**Intervention:** • Smoking cessation pharmacotherapy (including NRT, varenicline, bupropion and nortriptyline, or a combination or choice of these) and in which one or more intervention conditions received more intensive behavioural support than the control condition. In addition, the intervention could use different or additional types of

	therapy content (eg. Cognitive behaviour therapy, motivational interviewing). This had to involve person-to-person contact which could be face-to-face or by telephone. • If trials have more than one intervention condition, we compared the most intensive combination of behavioural support and pharmacotherapy to the control.
	Comparators: • Any level of support from minimal (e.g. written information provided as part of the medication prescription) to multisession counselling, but support must have been of a lower intensity (based on number or length of sessions) than that given to intervention participants.
Outcomes and methods of analysis	**Outcomes:** The primary outcome was cessation after at least 6 months of follow up. The strictest rates of cessation were used - such as sustained rather than point prevalence abstinence. Biochemical validated rates were used where available. Drop-out and losses to follow up was treated as continuing smoker.
	Methods of analysis: Quantitative analysis: treatment effect (relative risk) and meta-analysis. They calculated risk ratio and 95% CI for each study, and performed meta-analysis using a Mantel-Haenzel fixed effect model where appropriate.
Results	**Conclusions from systematic review** • Providing behavioural support in person or via telephone for people using pharmacotherapy to stop smoking has a small but important effect. Increasing the amount of behavioural support is likely to increase the chance of success by about 10% to 25%, based on a pooled estimate from 47 trials. Subgroup analysis suggests that the incremental benefit from more support is similar over a range of levels of baseline support. **Findings from studies. Key comparisons:** • *Comparison: Behavioural interventions as adjuncts to pharmacotherapy vs minimal behavioural intervention with pharmacotherapy.* There was evidence of a small but statistically significant benefit from more intensive support (RR 1.17, 95% CI 1.11 to 1.24, I^2= 18%, p<0.00001) for abstinence at longest follow-up. All but four of the included studies provided four or more sessions of support to the intervention group. Most trials used NRT. N = 18, 682. • In subgroup analyses, studies that provided at least four sessions of personal contact for the intervention and no personal contact for the control had slightly larger estimated effects (RR 1.25, 95% CI 1.08 to 1.45 I^2= 0%, p=0.0025; 6 trials, 3762 participants), although a formal test for subgroup differences was not significant. • Studies where all intervention counselling was via telephone (RR 1.28, 95% CI 1.17 to 1.41 I^2= 0% p<0.00001; 6 trials, 5311 participants) also had slightly larger effects, and the test for subgroup differences was significant, but this subgroup analysis was not pre-specified.

	• The quality of the evidence was judged to be high using the GRADE approach.
Limitations	**Identified by authors** • The review focused on the amount of behavioural support rather than the specific components, or the quality of delivery.
	Identified by developers • None.
Additional comments	**Comments** • The majority of studies were conducted after 2000. • Only 2 UK studies were included. **Relevance to Recommendations:** • Most of the studies were conducted in US and the settings were variable, and included secondary care. • The evidence relates to interventions that include pharmacotherapy. Additional behavioural support or more intensive behavioural support is likely to provide some additional benefits.
	Source of funding Nuffield Department of Primary Care Health Sciences, Oxford University, UK. NHS National Institute for Health Research, UK. Faculty of Medicine Marvin Burke Summer Studentship, Dalhousie University, Canada.

D.6 Digital media

Evidence table: Japuntich et al 2006

Study details	Population Intervention/comparison	Results	Conclusion and notes
Japuntich et al 2006 **• Review Quality** *[+]* **• Country** *USA* **Study design** • RCT **• Aim of study.** *To evaluate the efficacy of an Internet intervention, the Comprehensive Health*	**• Setting** *Two sites + home based (internet access)* *(N=134 Milwaukee & N=150 Madison, Wisconsin)* **• Population (demographics) N=284** *610 people applied via advertising (2001-2), screened for eligibility (via telephone); 284 selected, motivated to quit smokers, passed screening requirements (e.g. completing physical exam by nurse, inclusion/exclusion interview, carbon monoxide (CO) test, informed consent procedures; N=140 allocated to CHESS-SCRP* (DM), N=144 to control (Standard Smoking Cessation Care).* *Note: All participants given free study medication in exchange participation and up to US$100 to return for biochemical confirmation*	**• Outcome - smoking cessation (***abstinence***)** *Expecting higher abstinence rates with internet use as an adjunct to standard care versus standard care only.* *Overall there were no statistically significant between group differences in outcomes.* **Access to CHESS SCRP (internet) condition did not predict abstinence at:* *3 months (OR=1.13, 95% CI.64-1.98) or* *6 months (OR =1.48, 95% CI .66 2.62).* **At 3 months post quit (end of the treatment phase), 32 people (22.9%) internet group & 30 people (20.8%) in the control group were abstinent.*	**• Author conclusions** *A primary question addressed by this research was whether an Internet-based smoking cessation intervention could significantly augment the abstinence rates produced by brief smoking cessation counselling and pharmacotherapy.* *No significant effects were found in this comparison*

Study details	Population Intervention/comparison	Results	Conclusion and notes
*Enhancement Support System for Smoking Cessation and Relapse Prevention (*CHESS SCRP), as an adjuvant to standard care, smoking cessation treatment.* **• Follow up period** *3 months, 6 months* **• Funding** *National Cancer Institute Grant P50 CA084724. The bupropion SR used in this study was provided by GlaxoSmithKline.* ***Citation:** *Smoking cessation via the internet: a randomized clinical trial of an internet intervention as adjuvant treatment in a smoking cessation intervention. Japuntich SJ ; Zehner ME ; Smith SS ; Jorenby DE ; Valdez JA ; Fiore MC ; Baker TB ; Gustafson DH ; 2006 Nicotine & Tobacco Research Volume 8, Supplement 1 (December 2006) S59-S67*	*of abstinence.* **Table 1 Demographics** *(at recruitment)*: **4 cols:** *Variable, Mean(standard Dev): Exp: Control: Total* *Participant N 140 144 284* *Gender (% fem) 55.0 54.9 54.9* *Race (% White) 75.4 82.6 79.1* *Age, M (SD) 40.6 (12.4) 41.0 (11.8) 40.8 (12.1)* *Cigs per day, M (SD) 21.1 (9.5) 22.1 (10.2) 21.6 (9.9)* *Yrs smkng M (SD) 22.7 (12.1) 23.3 (12.3) 23.0 (12.2)* *No quit attmpts M (SD) 5.4 (12.5) 6.1 (11.1) 5.8 (11.8)* **Highest level education completed** *High school or less 5 (3.6%) 4 (2.8%) 9 (3.2%)* *High schl or GED 41 (29.5%) 40 (27.8%) 81 (28.7%)* *Some collg/tech schl 72 (51.8%) 68 (47.2%) 140 (49.6%)* *Collg/grad school 21 (15.1%) 31 (21.5%) 52 (18.4%)* **FTND, M (SD) 5.4 (2.1) 5.5 (4.4) 5.4 (2.1)* **CES-D, M (SD) 5.2 (4.7) 5.5 (4.4) 5.4 (4.6)* ** Note.* *CES-D, Center for Epidemiological Studies Depression Scale;* *FTND, Fagerstrom Test for Nicotine Dependence* **• Intervention - digital media component** *Experimental condition + standard SC (Bupropion, counselling), a free study computer, (dial-up) and 12 weeks (90 days) of access to the CHESS SCRP Web site, participants were encouraged to access once per day. Full instructions and orientation were provided (see paper for further details). Participants in the CHESS SCRP condition received CHESS SCRP access for 90 days. Participants were instructed to log onto CHESS SCRP daily, if a week without logging onto CHESS SCRP, staff telephoned them (up to three times per week) and reminded them to log in.*	**At 6 months post quit date, 21 people (15.0%) in internet group and 17 people (11.8%) in control group were abstinent.* *How much participants used the internet program* ** hours internet use per week & abstinence significantly related at:* *3 months (OR 1.79, 95% CI 1.25-2.56)* *6 months (OR 1.59, 95% CI 1.06-2.38),* *People with more logged on hours - greater internet use - were more likely to be abstinent.* *Additional co-variate analysis : Because individuals were not randomly assigned to levels of use, it is undetermined whether more use caused participants to quit at higher rates. It is possible that a third variable such as quitting history, past quitting success, or success expectations caused both use and cessation success. Controlling for these variables, further analyses indicated extent of use per week was still significantly related to abstinence (3 months: OR=2.10, 95% CI 1.36-3.25; 6 months: OR =2.13, 95% CI 1.25-3.61).* *Older participants were more likely to be abstinent* *Cessation rates did not differ by gender, education, or race/ethnicity; but differed by age at 3 months post quit, but not at 6 months (OR=1.026,95% CI, 1.002-1.05).* *Relapse prevention* *Access to CHESS SCRP did not predict abstinence at 3 or 6 months. A non-significant trend for programme users to maintain abstinence was reported as 3 months post quit OR=1.07, 95% CI .54-2.14 and 6 months post quit (OR=1.66,95% CI .76-3.63).*	*(internet+std care vs. std care).* *Authors note similar negative outcomes as other similar research, but speculate If similar effect sizes were found in population-based applications of Web-based cessation interventions, it may be possible to observe meaningful public health impacts. Authors report participants used CHESS SCRP multiple times per week, averaging 6 hr+ of use per participant. This shows clearly that smokers will, under highly controlled circumstances, use an Internet cessation treatment. It is uncertain, however, whether less motivated individuals, such as those who would not sign up for a cessation research program, would use an Internet intervention to the same degree. Also, intervention use in this research program may have been*

Study details	Population Intervention/comparison	Results	Conclusion and notes
	CHESS SCRP is structured web-based internet program, organised into 4 easy to read sections offering emotional support, problem solving assistance, access to SC counsellors and clinical psychologists. It is designed to include information only on clinically validated treatments for smoking cessation. Participants logging onto CHESS SCRP complete a brief entry (check-in) assessment which produces a graph of the users smoking history and withdrawal levels over the course of the quit attempt and recommends different articles or other services to the user based on his or her responses to the check-in (e.g., smokers reporting depression were encouraged to use the Cognitive Behavioural Therapy service). (See paper for full description) • **Intervention(s) - non digital media components** *Counselling sessions, plus a supply of bupropion SR 150 mg (provided by GlaxoSmithKline), following standard procedure and dosage (e.g. taking 7-10 days prior quit day, bupropion SR 150 mg once each morning for 3 days followed by bupropion SR 150 mg twice daily for 9 weeks).* *Participants came to follow-up visits 2, 4, 6, 8, and 12 weeks after quit date.* *These follow-up visits assessed tobacco use, use of therapeutic aids for smoking cessation (e.g. bupropion SR, nicotine replacement, and Internet cessation services), and vital signs. In addition, participants completed a variety of questionnaire measures at each visit. No counselling occurred during these visits. Participants were*	*Authors analyzed data only from participants not smoking (n=134) at first follow-up visit after quit day.*	*enhanced by reminder telephone calls urging participants to use the system; the protocol allowed a maximum of three such calls per week, for every week the participant did not log in at least once.* • **Analyst conclusions** *Analyst in general agreement with authors. A carefully planned and well conducted study of an intense intervention to test the efficacy of a computer based programme under controlled conditions as an adjunct to standard smoking cessation care. The intervention schedules were hard to follow (use of a table format would have helped).* *Not mentioned here are author's caveats about cost of accessing internet in 'real world', given age of study, this may no longer apply (original study*

Study details	Population Intervention/comparison	Results	Conclusion and notes
	followed up by telephone monthly from 4 months to 12 months after their quit date. At both the 6- and 12-month telephone follow-ups, abstinent participants were asked to come to the study site for CO measurement. Follow-up telephone calls assessed cigarette smoking, other tobacco use, smoking cessation treatment use, depression and suicidality, withdrawal and motivation to quit. **• Comparator** *Control condition - 9 weeks of twice daily bupropion SR (150 mg), three brief individual counselling sessions, and five follow-up visits.* .**Outcomes and methods of analysis** **• Outcomes** *Smoking status was the main outcome measure, 7-day point prevalence. Biochemical verification using an expiratory breath CO test value of less than 10 ppm considered not smoking, greater than 9 ppm non-abst. Participants who did not respond to follow-up contacts were considered smokers* **• Methods of analysis** *Intention-to-treat approach, making the assumption that non-responders were continuing smokers.*		*used dial up) but authors' assertion about access to reliable information about smoking cessation still holds.* *Authors did not report methods of randomisation or allocation concealment.*

Evidence table: Naughton et al 2014

Study details	Population Intervention/comparison	Results	Conclusion and notes
Naughton et al 2014 **• Review Quality** *[++]* **• Country** *England, UK*	**• Setting** *Primary care: 32 general practitioner surgeries* **• Population (demographics)** *N=602 adults met inclusion criteria, randomised to 1 of 2 conditions. Intervention group n=299, Comparison group n=303. Participants mean age 41.8 (SD=13), and 52.7% were female.*	**• Outcome - smoking frequency** *There were no significant between-group differences in 2-week point prevalence abstinence at the 8-week primary end-point [control 40.3%, iQuit 45.2%; odds ratio (OR) = 1.22, 95% CI = 0.88–1.69] or in any secondary short-*	**• Author conclusions** *Longer-term abstinence at 6 months was clinically and statistically significantly higher among iQuit participants*

Study details	Population Intervention/comparison	Results	Conclusion and notes
Study design • RCT **• Aim of study.** *To estimate the short-term effectiveness, feasibility and acceptability of a smoking cessation intervention (iQuit system) comprising tailored printed and short Message Service (SMS) text message self-help delivered as an adjunct to cessation support in primary care to inform the design of a definitive trial* **• Follow up period** *2, 4 and 8 weeks and 6 months* **• Funding** *National Institute for Health Research School for Primary Care Research (SPCR), GP practice costs*	*Two-thirds smoked within 30 minutes of waking and the mean daily smoking rate was 18.3 (SD = 8.0) cigarettes. Significance of baseline between group demographic differences was not reported.* **• Eligibility criteria** *General practices with at least one SCA (primary care nurse or healthcare assistant, a nursing auxiliary under the guidance of a qualified healthcare professional) trained to give 'level 2' smoking cessation advice with internet and printer access from their consultation room(s) were eligible. Patients were eligible for inclusion if they were: a current smoker; able to read English and provide written informed consent; willing to set a quit date within 14 days after randomization; aged 18–75 years; have a mobile phone and able to send/receive text messages; no in another smoking cessation programme; and not using smoking cessation medications at randomization date.* **• Intervention - digital media component** *Tailored printed and SMS text message self-help - designed to be used by Practice nurses or smoking cessation advisors: Generates a highly tailored report and initiates a 90 day programme of automated tailored text messages to the smokers mobile phone (self -help tool)* **• Intervention(s) - non digital media components** *Smoking cessation - usual care.* **• Comparator** *Usual care - smoking cessation: level 2 smoking cessation advice delivered by Smoking Cessation Advisors (discussion about smoking habits, history, measurement of expired air carbon monoxide. brief*	*term abstinence outcomes. The intervention group performed statistically significantly better than the comparison group for: 6-month prolonged abstinence at 6 months (control 8.9%, iQuit 15.1%; OR = 1.81, 95% CI = 1.09–3.01) 6-month continuous abstinence (control 6.3%, iQuit 11.4%; OR = 1.92, 95% CI = 1.07–3.45).* **• Outcomes - acceptability of intervention** *Most intervention group participants reported: 1) advice report useful (79.2%, 95%CI - 73.1%-84.%), 2) easy to understand (88.0%, 95%CI - 82.8%-91.8%) 3)that it helped them to quit smoking (65.2%, 95% 58.4%-71.4%). 4) text messages an acceptable way of receiving smoking cessation support (67.7%), 5) useful (64.1%), 6) easy to understand (93.7%) and just fewer than half found 7) helped them to quit smoking (44.8%), 8) annoying to some extent (25.5%). Of intervention participants, 1) 18.9% sent a STOP text message, on average 52.5 (SD = 18.9) days into the 90-day programme. Around one-quarter of those who sent a STOP message (representing approximately 5% of all intervention participants) reported doing so due to annoyance.*	*compared with controls - there was a benefit to receiving iQuit support for the quit attempt planned at enrolment. No evidence of a short-term benefit of iQuit support. iQuit support was acceptable to most participants and was feasible to deliver within the context of a primary care consultation.* **• Analyst conclusions** *Agree with author conclusions, a well-conducted feasibility study, to test the protocol for a larger trial.*

Study details	Population Intervention/comparison	Results	Conclusion and notes
(NHS Service support costs) were provided by local research network. A.T.P was supported by NIHR Biomedical research centre based at Guy's and St Thomas' NHS Foundation Trust and King's College London	*advice to quit, setting a quit date within 14 days, pharma options, prescription and arranging a follow-up visit plus opportunity for multiple follow-up visits.* **Outcomes and methods of analysis** • **Outcomes** *Primary: self-reported 2 week point prevalence of abstinence at 8 week follow-up Secondary: CO-verified abstinence at 4-week follow-up from quit date for at least 2 weeks. Self-reported 3-month prolonged abstinence at 6-month follow-up from randomization date. 6-month prolonged abstinence at 6-month follow-up and a strict continuous abstinence measure using all outcome time points: CO-validated 2-week point prevalence abstinence at 4 weeks, 4-week point prevalence abstinence at 8 weeks and 6-month prolonged abstinence at 6 months* • **Methods of analysis** *Groups were compared using χ2 tests and logistic regression analysis for binary outcome measures, independent t-tests, analysis of variance and linear regression analysis for continuous measures and Fisher's exact test and 95% CI for between-group proportions. Single arm proportions were estimated with exact 95% CI using the binomial distribution. The smoking outcome analyses were intention-to-treat, participants lost to follow-up assumed to be smoking. Sensitivity analyses undertaken using a range of less severe assumptions, namely a complete-case analysis and relaxation of the 4-week abstinence definition*		

Evidence table: Pakhale et al 2015

Study details	Population Intervention/comparison	Results	Conclusion and notes
Pakhale et al 2015 **• Review Quality** *[+]* **• Country** *Canada* **Study design** • pilot RCT **• Aim of study.** *Assess the feasibility and potential effectiveness of a modified version of the Ottawa Model for Smoking Cessation in an outpatient respirology clinic.* **• Funding** *Department of Medicine, University of Ottawa, University of Ottawa Heart Institute for funding this project* **• Follow up period** *26 to 52 weeks*	**• Setting** *Respirology Clinic at the Ottawa Hospital.* **• Population (demographics)** *Intervention group n=23, comparison group n=26 All participants: Mean age= 50.9+/-10.4 (Control); 48.6+/-12.3 (Intervention); 49% were male Any baseline differences between the intervention and comparison groups were not statistically significant. Loss to follow-up was not significantly different between groups.* **• Eligibility criteria** *Smokers aged 18 years or over, attending respirology clinic and willing to set a quit date within one month of randomisation were eligible. Subjects with a life expectancy <2 years, and individuals unable to speak English or French were excluded.* **• Intervention - digital media component** *Participants were registered to an automated calling system that made nine calls scheduled seven days before their set quit date, and three, 14, 30, 60, 90, 120, 150 and 180 days after. The system made a maximum of two daily call attempts over four days. During calls, participants were asked about their smoking status, confidence in being able to remain smoke-free.* **• Intervention(s) - non digital media components** *Standard care plus brief counselling session, a $110 voucher to purchase smoking cessation pharmacotherapy* **• Comparator** *Standard care: Smoking cessation advice, a brochure and a prescription for smoking cessation medication if requested.* **Outcomes and methods of analysis** **• Outcomes** *Self-reported smoking status, not biochemically verified: Self-reported smoking status was the primary indicator of effectiveness and was obtained at 26 to 52 weeks. Participants were asked to consider their smoking behaviour over the past month and respond 'yes' or 'no' to the question "Do you still smoke?"*	**• Outcome - smoking frequency** *Self-reported smoking status: data at 26 to 52 weeks was available for 32 participants. On average, these were collected 234.4 days (33 weeks) after baseline, with no significant difference between study groups. Non-smoker status was 18.2% in the intervention group compared with 7.7% in the control group. The OR for self-reported non-smoker status was 2.36 (95% CI 0.39 to 14.15). Observed differences between groups were not statistically significant (P=0.654).* **• Outcomes** - uptake of services *Received and used $110 voucher: Twenty (86.9%) of the 23 intervention group participants used their $110 voucher to purchase pharmacotherapy; the mean (± SD) amount spent on pharmacotherapy was $98.70±36.50 Reach of automated calls: The mean number of completed automated calls per participant was 3.5±3.2. Seven (14.3%) responded to 0 calls, five (10.2%) responded to one to three calls, five (10.2%) between four and six calls, and six (12.2%) between seven and nine calls. The proportion of participants reached decreased over time from 52.2% to 26.1%. Eleven (22.4%) participants received at least one nurse counselling call and the mean number of times each of them was counselled by a nurse was 2.0±1.1 (range one to nine). More than 50% of participants*	**• Author conclusions** *The intervention was associated with higher quit rates than the standard care, however these differences were not statistically significant. The present pilot was not powered to produce statistically conclusive results. This feasibility study was limited to a single site and, therefore, findings may not be generalizable to a wider population of respirology patients in different settings.* **• Analyst conclusions** *Broadly in overall agreement with author conclusions. The intervention appears to be feasible. However some caution should be given to interpreting results. It had been intended to collect a carbon monoxide (CO) samples to verify self-report. Clinic attendance for this purpose was inconvenient for many participants, resulting in missing data. A decision was therefore made*

Study details	Population Intervention/comparison	Results	Conclusion and notes
	Feasibility: Feasibility indicators included recruitment and retention rates, and adherence to intervention components (voucher use and response rates to automated and nurse counselling calls). **• Methods of analysis** *Comparisons between groups were performed using using χ2 tests, Fisher's exact tests, Student's t tests and Mann-Whitney U tests, depending on the distribution and nature of the data. An effectiveness analysis on self-reported smoking status was conducted using a Fisher's exact test and an OR was computed adjusting for clinically significant variables. All participants, with the exception of those who were deceased or had moved to an untraceable address, were included in the analysis. Participants with missing self-reported smoking status data at 26 to 52 weeks were considered to be smokers according to the Russell Standard.*	*flagged during the automated calls subsequently received counselling. Four (17.4%) participants opted out of the automated calling system Use of Pharmacotherapy: The completion rate of the monthly telephone calls during which data regarding pharmacotherapy use were collected ranged from 32.0% to 73.9% across groups and over time no significant differences in pharmacotherapy use between study groups*	*to forego biochemical confirmation and to collect self-reported smoking status using telephone contact or by meeting participants at their next scheduled clinic visit. These changes resulted in delays, and outcome data presented in the present article were collected between 26 and 52 weeks.*

Appendix E: Excluded Studies

E.1 List of excluded studies

Study	Reason for Exclusion
Apollonio D, Philipps R, Bero L. Interventions for tobacco use cessation in people in treatment for or recovery fromsubstance abuse. Cochrane Database of Systematic Reviews 2012, Issue 12.	Review protocol
Barth J, Jacob T, Daha I, Critchley JA. Psychosocial interventions for smoking cessation in patients with coronary heart disease. Cochrane Database of Systematic Reviews 2015, Issue 7.	Setting excluded (primarily secondary care)
Baxi R, Sharma M, Roseby R, Polnay A, Priest N, Waters E, Spencer N, Webster P. Family and carer smoking control programmes for reducing children's exposure to environmental tobacco smoke. Cochrane Database of Systematic Reviews 2014, Issue 3.	Not primarily cessation. Not all participants fall into a target group of interest
Cahill K, Lancaster T. Workplace interventions for smoking cessation. Cochrane Database of Systematic Reviews 2014, Issue 2.	Setting excluded (workplace)
Carson KV, Brinn MP, Peters M, Veale A, Esterman AJ, Smith BJ. Interventions for smoking cessation in Indigenous populations. Cochrane Database of Systematic Reviews 2012, Issue 1.	Not all participants fall into a target group of interest
David SP, BergenAW,MunafòMR, Schuit E, BennettDA, PanagiotouOA.Genomic analysis to guide choice of treatment for smoking cessation. Cochrane Database of Systematic Reviews 2015, Issue 8.	Review protocol
Hartmann-Boyce J, Lancaster T, Stead LF. Print-based self-help interventions for smoking cessation. Cochrane Database of Systematic Reviews 2014, Issue 6.	Print-based self-help

Study	Reason for Exclusion
Jeyashree K, Kathirvel S, Shewade HD, Kaur H, Goel S. Smoking cessation interventions for pulmonary tuberculosis treatment outcomes. Cochrane Database of Systematic Reviews 2016, Issue 1.	Setting excluded (primarily secondary care)
Khanna P, Clifton AV, Banks D, Tosh GE. Smoking cessation advice for people with serious mental illness. CochraneDatabase of Systematic Reviews 2016, Issue 1.	Setting excluded (primarily secondary care)
Lancaster T, Stead LF.Mecamylamine (a nicotine antagonist) for smoking cessation. Cochrane Database of Systematic Reviews 1998, Issue 2.	Wrong intervention (nicotine antagonist)
Lancaster T, Stead LF. Silver acetate for smoking cessation. Cochrane Database of Systematic Reviews 2012, Issue 9.	Wrong intervention (silver acetate)
Lindson-Hawley N, Aveyard P, Hughes JR. Reduction versus abrupt cessation in smokers who want to quit. Cochrane Database of Systematic Reviews 2012, Issue 11.	Harm reduction
van der Meer RM, Wagena E, Ostelo RWJG, Jacobs AJE, van Schayck CP. Smoking cessation for chronic obstructive pulmonary disease. CochraneDatabase of Systematic Reviews 2001, Issue 1.	Setting excluded (primarily secondary care)
van der Meer RM, Willemsen MC, Smit F, Cuijpers P. Smoking cessation interventions for smokers with current or past depression. Cochrane Database of Systematic Reviews 2013, Issue 8.	Setting excluded (primarily secondary care)
Pool ERM, Dogar O, Siddiqi K. Interventions for tobacco use cessation in people living with HIV and AIDS. Cochrane Database of Systematic Reviews 2014, Issue 5.	Review protocol
Park EW,Tudiver FG,Campbell T. Enhancing partner support to improve smoking cessation. CochraneDatabase of Systematic Reviews 2012, Issue 7.	Not all participants fall into a target group of interest
Steed L, Kassavou A,Madurasinghe VW, Edwards EA, Todd A, Summerbell CD,NkansahN, Bero L,Durieux P, Taylor SJC, Rivas C,Walton RT. Community pharmacy interventions for health promotion: effects on professional practice and health outcomes. Cochrane Database of Systematic Reviews 2014, Issue 7.	No relevant outcomes reported.
Stead LF, Lancaster T. Interventions to reduce harm from continued tobacco use. Cochrane Database of Systematic Reviews 2007, Issue 3.	Harm reduction
Stead LF, Hartmann-Boyce J, Perera R, Lancaster T. Telephone counselling for smoking cessation. Cochrane Database of Systematic Reviews 2013, Issue 8.	Quitlines out of scope
Thomsen T, Villebro N, Møller AM. Interventions for preoperative smoking cessation. Cochrane Database of Systematic Reviews 2014, Issue 3.	Setting excluded (primarily secondary care)
Tsoi DT, Porwal M, Webster AC. Interventions for smoking cessation and reduction in individuals with schizophrenia. Cochrane Database of Systematic Reviews 2013, Issue 2.	Setting excluded (primarily secondary care)
van Eerd E, van der Meer RM, Reda AA, van Schayck CP, Kotz D. Smoking cessation in smokers with chronic obstructive pulmonary disease. CochraneDatabase of Systematic Reviews 2013, Issue 9.	Review protocol
Zeng L, Yu X, Yu T, Xiao J, Huang Y. Interventions for smoking cessation in people diagnosed with lung cancer. Cochrane Database of Systematic Reviews 2015, Issue 12.	Setting excluded (primarily secondary care)

Appendix F:Expert testimonies

Expert testimony is an important source of evidence for guidelines. Experts may be called upon when evidence from published literature is insufficient, or where there are gaps in published evidence meaning that review questions may not be fully answered.

The committee identified a gap in the evidence base for the question on advice on the use of e-cigarettes and so requested expert testimony to inform committee discussions. Three experts were selected, one to provide an overiew of research evidence on effectiveness (author of a subsequently publiushed Cochrane review) and two to discuss current knowledge on use of e-cigarettes.

The committee also agreed that expert testimony was the best avalable evidience with which the recommendation on stop smoking services could be updated and so two experts were sought to provide testimony on this topic.

As evidence from expert testimony may be more susceptible to bias than evidence from high quality published literature, the committee were given the opportunity to ask questions about methods or other issues to establish a better understanding of possible biases and applicability to the subject of the guideline.

F.1 Expert testimony 1 – e-cigarettes

Expert testimony to inform NICE guideline development

Section A: Developer to complete	
Name:	Jamie Hartmann-Boyce
Role:	Research Associate
Institution/Organisation (where applicable):	Cochrane Tobacco Addiction Group Nuffield Department of Primary Care Health Sciences
Guideline title:	NICE Smoking cessation interventions update PH1 PH10
Guideline Committee:	PHAC F
Subject of expert testimony:	Latest Cochrane evidence evaluating the safety and effect of using electronic cigarettes for smoking cessation
Evidence gaps or uncertainties:	RQ6 The role of e-cigarettes in smoking cessation

Can electronic cigarettes help people stop smoking, and are they safe to use for this purpose?

Section B: Expert to complete
Summary testimony:

About Cochrane

Cochrane is a global independent network of researchers, professionals, patients, carers, and people interested in health.

Cochrane produces reviews which study all of the best available evidence generated through research and make it easier to inform decisions about health. These are called systematic reviews.

Cochrane is a not-for-profit organization with collaborators from more than 130 countries working together to produce credible, accessible health information that is free from commercial sponsorship and other conflicts of interest. Our work is recognized as representing an international gold standard for high quality, trusted information.

Background

Electronic cigarettes (ECs) are electronic devices that produce an aerosol (commonly referred to as vapour) that the user inhales. This vapour typically contains nicotine without most of the toxins smokers inhale with cigarette smoke. ECs have become popular with smokers who want to reduce the risks of smoking. This review aimed to find out whether ECs help smokers stop smoking, and whether it is safe to use ECs to do this.

Study characteristics

This is an update of a previous review. The first review was published in 2014 and included 13 studies. For this update, we searched for studies published up to January 2016 and found 11 new studies. Only two of the included studies are randomized controlled trials and followed participants for at least six months. These provide the best evidence. The remaining 22 studies either did not follow participants for very long or did not put people into treatment groups so could not directly compare ECs with something else. These studies can tell us less about how ECs might help with quitting smoking but can tell us about short-term safety. The two randomized trials, conducted in New Zealand and Italy, compared ECs with and without nicotine. We judged these studies to be at low risk of bias. In one study, people wanted to quit smoking, while in the other study they did not. The trial in people who wanted to quit smoking also compared ECs to nicotine patches.

Key results

Combined results from two studies, involving 662 people, showed that using an EC containing nicotine increased the chances of stopping smoking in the long term compared to using an EC without nicotine.

We could not determine if EC was better than a nicotine patch in helping people stop smoking, because the number of participants in the study was low. More studies are needed to evaluate this effect.

The other studies were of lower quality, but they supported these findings. None of the studies found that smokers who used EC short- to mid-term (for two years or less) had an increased health risk compared to smokers who did not use ECs.

Quality of the evidence

The quality of the evidence overall is low because it is based on only a small number of studies, although these studies were well conducted. More studies of ECs are needed. Some are already underway.

References to other work or publications to support your testimony' (if applicable):
Hartmann-Boyce J, McRobbie H, Bullen C, Begh R, Stead LF, Hajek P. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews 2016, *Issue* 9. *Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub3.*

F.2 Expert testimony 2 – e-cigarettes

Expert testimony to inform NICE guideline development

Section A:	
Name:	Professor Peter Hajek
Role:	Professor of Clinical Psychology
Institution/Organisation (where applicable):	Wolfson Institute of Preventive Medicine Queen Mary University of London
Guideline title:	Smoking cessation interventions and services (update)
Guideline Committee:	PHAC F
Subject of expert testimony:	The role of electronic cigarettes in smoking cessation
Evidence gaps or uncertainties:	RQ6 The role of e-cigarettes in smoking cessation

Section B: Expert to complete
Summary testimony:
E-cigarettes The role of electronic cigarettes (EC) in reducing smoking can be evaluated on the population level or in a narrower context of treating smokers seeking help. On the population level, data are needed on changes in smoking prevalence in countries that allow and countries that ban EC. Regarding single countries data, the increase in popularity of vaping has been accompanied by reduction in smoking, with large numbers of smokers successfully switching to vaping in countries where vaping is allowed. Over 6 million smokers quit with the help of EC in Europe. UK has derived a particularly strong benefit from EC so far. Preliminary 2015 data suggest that there are some 800,000 ex-smokers in the England who successfully switched to vaping and another 640,000 who used to smoke and vape has now stopped both. In summary, vaping has started to replace smoking on the population level, although the forthcoming TPD regulation is likely to slow down product development and EC adoption. In the treatment context, only 2 RCTs with long-term outcomes evaluated EC efficacy. The results were positive but limited. Because of the small number of trials and obsolete EC products they used, the confidence in the effect, especially in its size, is low. Observational studies suggest that smokers quitting with the help of EC have higher success rates than those trying alternatives, but non-randomised studies are subject to self-selection bias. Randomised trials are needed that compare the efficacy of free choice of EC with effects of existing treatments. Including an offer of a 'starter pack' EC within the English stop-smoking services is likely to increase their attractiveness and reach and may increase their efficacy.
References to other work or publications to support your testimony' (if applicable):

F.3 Expert testimony 3 – e-cigarettes

Expert testimony to inform NICE guideline development

Section A: Developer to complete	
Name:	David W Bareham
Role:	Specialist Respiratory Physiotherapist
Institution/Organisation (where applicable):	Lincolnshire Community Health Services NHS Trust
Guideline title:	Smoking cessation interventions and services (update)
Guideline Committee:	PHAC F
Subject of expert testimony:	The role of e-cigarettes in smoking cessation
Evidence gaps or uncertainties:	RQ6 The role of e-cigarettes in smoking cessation
Section B: Expert to complete	
Summary testimony:	The role of e-cigarettes in smoking cessation

Authored by David Bareham, Specialist Respiratory Physiotherapist, Lincolnshire Community Health Services, Simon Capewell, Professor of Clinical Epidemiology, University of Liverpool, and Professor Martin McKee, Professor of European Public Health, LSHTM.

A Summary of the Presentation given by David Bareham to the National Institute for Health and Care Excellence Public Health Advisory Committee, on 13.10.16.

All views in this presentation were/are of the authors alone, and do not necessarily reflect those of their employers.

This paper summarises a presentation made to the National Institute for Health and Care Excellence Public Health Advisory Committee which seeks to resolve some of the conflicting views.

1. Smoking Cessation

Our position, in view of the current evidence, is that e-cigarettes should not be *routinely* recommended for smoking cessation by clinicians.

The role of electronic cigarettes (e-cigarettes) in reducing the burden of smoking related harm has generated considerable controversy. A number of English organisations have expressed views that are somewhat more favourable to these products than those found elsewhere. The World Health Organization and US Food and Drug Administration, as well as leading European, American, and international professional bodies, have all expressed considerable caution.

The diversity of views is present even among those who have indicated general support for the greater use of e-cigarettes in Smoking Cessation. For example,

McNeill, while conceding that more data are required, still states that e-cigarettes *should be recommended* as quitting aids by clinicians (1).
In contrast, Bullen, who has also expressed support for greater use of e-cigarettes (2), writing as co-author of the *Cochrane Review* on e-cigarettes (3), argues that:

- *"health care professionals should communicate that there is limited evidence on the types or concentrations of potentially harmful chemicals they are exposed to when they use these products or their long-term efficacy and safety" (2), and that*

- *"for smokers who have been unable to quit by using standard treatment or for smokers unlikely to try standard medications, health professionals could consider discussing the option of trying an EC" (2)*

These differences are also seen among key U.K. organisations. For example, Public Health England, referring to their effectiveness as smoking aids, state that they "appear to be effective", while, the British Heart Foundation (BHF) state currently that "There is a lack of empirical research regarding the effectiveness of e-cigarettes as a smoking cessation aid . . .". Other recent influential international reviews concur with the BHF analysis (4; 5).
The "Gold Standard" (6) Cochrane Review (3) found only two Randomised Controlled Trials to include in its meta-analyses, concluding that:

- *"under GRADE system we rated overall quality of the evidence for our outcomes as 'low' or 'very low' " and*

- *"The one study that compared EC to nicotine patch found no significant difference in six-month abstinence rates"*

That single Randomised Controlled Trial (7) when critically appraised, elucidated the following comments from the authors:

1) *"Achievement of abstinence was substantially lower than we anticipated for the power calculation . . ."*

2) *". . . thus we had insufficient statistical power to conclude superiority of nicotine e-cigarettes to patches or to placebo e-cigarettes."*

Other important methodological issues include:

3) The Authors confirmed they were "optimistic" about effect size and estimates of abstinence, hence the reduced statistical power when the trial results became available

4) There was a high loss to follow-up in the patches group; those allocated to the patches group may have been disappointed, as they may well have tried these before, and failed, and so dropped out . . .

5) E-Cigarettes were couriered to participants; however, those allocated patches were mailed a voucher to exchange for NRT at a pharmacy: there was a clear difference in quality of administration.

It therefore appears evident that:
Efficacy data of the basic quality required to substantiate recommendation is *currently* absent.

We thus concur with The World Health Organisation's recent assessment, based on a series of reviews conducted by methodological experts, who had not previously expressed a view on e-cigarettes:

"Whether ENDS/ENNDS can do this job {promote effective smoking cessation} is still a subject of debate between those who want their use to be swiftly encouraged and endorsed on the basis of available evidence, and others who urge caution given the existing scientific uncertainties as well as the performance variability of products and the diversity of user behaviour." (8)

The main study cited in support of the use of e-cigarettes for smoking cessation in England is that by Brown et al (9). Yet it is a cross sectional survey, that can only establish *"association at most, not causality" (10).* Moreover, given the known potential for biases in reporting, it is very important that biochemical verification of smoking cessation, using cotinine measurement, is considered. The study by Brown et al (9) concedes that: "In randomized trials, this {lack of biochemical verification} would represent a serious limitation because smokers receiving an active treatment often feel social pressure to report abstinence." Yet the authors then dismiss this concern, arguing that "However, in population surveys the social pressure and *the related rate of misreporting is low and it is generally considered acceptable to rely upon self-reported data."(emphasis added)*. This view is justified by reference to a study of Canadian smokers (11). However, this paper highlights that *there are potentially important differences between responders of different countries.* Thus, as West et al noted in "Can We Trust National Smoking Prevalence Figures? Discrepancies between Biochemically Assessed and Self-Reported Smoking Rates in Three Countries" (12), "Underestimation of smoking prevalence was minimal in the United *States but significant in England* and Poland" (emphasis added). Consequently, we believe that this provides further reason to be cautious about the interpretation of the study by Brown et al., given the potential for social desirability bias. It was surprising that, given the overlap and authorship, the last of these studies was not cited in Brown et al.
Perhaps more concerning have been recent examples where inappropriate claims implying causality have been made on the basis of evidence from cross sectional surveys. A Cancer Research UK poster, claimed superiority of e-cigarettes alone over NRT alone (13), by merely citing the Brown et al study. Potentially inappropriate "lumping" occured of the Cochrane Systematic Review data (3) with the Brown et al cross sectional data (10) to produce one figure for cessation efficacy of e-cigarettes compared to no aid or bought licensed nicotine products i.e.:

"Evidence from RCTs and from surveys in England indicate that using an e-cigarette in a quit attempt increases the probability of success on average by approximately 50% compared with using no aid or LNP bought from a shop." (14)

This approach, combining the Cochrane Review analysis of 2 RCTs, which identified only low or very low Grade outcomes and insufficient evidence to conclude superiority of electronic cigarettes over patches, with the Brown et al cross sectional study, from which, clearly, causality cannot be claimed, appears erroneous and potentially misleading.

A further critique of claiming causality from a cross sectional survey (15) has recently been published, and additional comment and review from a Cochrane

Review author, and colleague, regarding the predictable but important caveats and limitations of these studies in relation to electronic cigarettes, further highlights limitations of published efficacy data (2). Furthermore, when recent claims are made from a leading e-cigarette advocate/academic arguing: "Why Anecdotal Evidence Proves that Electronic Cigarettes ARE Helpful for Smoking Cessation" (16), while still highlighting that robust RCTs are required, the current scientific data supporting the efficacy of electronic cigarettes appears profoundly weak and fragile. However, it is, of course, essential, as part of the "Therapeutic Relationship" and a clinician's Code of Professional Conduct, to be empathetic, and to value and celebrate the success of individuals quitting smoking by any means.

In summary, the evidence that e-cigarettes are effective in smoking cessation in England appears decidedly weak.

2. Safety

We now turn to the issue of safety of e- cigarettes. As noted in the recent statement by a co-author of the Cochrane Review:
". . . health care professionals should communicate that there is limited evidence on the types or concentrations of potentially harmful chemicals they are exposed to when they use these products or their long-term efficacy and safety" (2)
Again quoting from a report co-authored by those who support wider use of e-cigarettes, we read that: *"e-cigarettes are unlikely to be harmless ". . ." long term use is likely to be associated with long term sequelae, including an increased risk of chronic obstructive pulmonary disease, lung cancer, possibly cardiovascular disease, and some other long term conditions associated with smoking"(17).*
We concur, and believe that there is an urgent need to provide appropriate health warnings for patients. Furthermore, the precise form of wording should take account of the full range of evidence, including that from a group of expert toxicologists (18) who have noted that:

" . . . Public Health England and the Royal College of Physicians in the UK, largely relied on expert opinion and where evidence was considered it largely focused on studies of vaping aerosol and e-liquid composition with relatively few biomarker studies . . .".

Their subsequent analysis of the few recent relevant biomarker studies currently available reveals a ". . . very diverse range of results . . . but all suggest lower levels of risk for vapers compared to tobacco smokers". However, "preliminary evidence . . . suggests that the effect of vaping on four other inflammatory markers of likely relevance to cardiovascular disease (CVD) and respiratory disease may be at least half that of tobacco smoking" and "The results for cancer-related toxicants were variable, from 0% to 23% of the levels observed for tobacco smokers, with most studies reporting between 14% and 23% – a substantial level of exposure. But it is plausible that some of these toxicants could be due to unreported dual use with smoked tobacco (and even exposure to second hand smoke)."

Other recent expert toxicological opinion (19) takes a more uncompromising line, arguing that for Public Health England and the Royal College of Physicians to postulate that e-cigarettes are a "low risk" product is: "*in the light of current*

knowledge, *a reckless and irresponsible suggestion".* The authors state that the PHE/RCP view:

"ignores the possibilities that users might be repeatedly exposed to hitherto undetected contaminants and by-products, as well as to carcinogenic chemicals, or their precursors (which have been detected in solvent extracts and vapours, and which are derived from tobacco during solvent extraction or generated during solvent heating), that can have effects at very low dose levels, following repeat exposures, which can occur without clear threshold doses, thus necessitating zero-dose extrapolation."

Furthermore, regarding nicotine, while nicotine is not currently categorised as a carcinogen by the International Agency for Research on Cancer (IARC), it has recently stated that investigation into the inhalation of nicotine via electronic cigarettes is a "High Priority". This is subsequent to new evidence elucidating: "the potential for nicotine to cause DNA damage" and that "exposure to nicotine has been shown to inhibit apoptosis, and stimulate cell proliferation and angiogenesis . . ." (20).
Very recent ex-vivo data, furthermore, has suggested that "E-cigarette use results in suppression of immune and inflammatory-response genes in nasal epithelial cells similar to cigarette smoke" (21).

In summary, while there is still great uncertainty, it is overwhelmingly clear that the toxicity of e-cigarettes is far from being appropriately understood.

In conclusion, on the basis of the existing data, it cannot be concluded that e-cigarettes are effective for smoking cessation, while there is also considerable evidence, albeit subject to some of the same limitations as that cited in support of e-cigarettes, that their use is likely to reduce the propensity to quit (36). In addition, there are solid grounds for concern about the long term health effects to users. In these circumstances, potential users, clinicians & policy makers cannot make fully informed choices regarding the use of e-cigarettes.
We therefore suggest that the Precautionary Principle should be applied until further data demonstrates more convincing efficacy and safety. The National Institute for Health and Care Excellence promotes evidence-based medicine, not scientific presumption, and should not currently be recommending the routine use electronic cigarettes for smoking cessation.
3. Additional Issues Generated During the Subsequent Committee Discussion
The content of the presentation was specifically to address the title that had been given: the role of e-cigarettes in smoking cessation. It was, therefore, limited to the scientific evidence currently regarding their efficacy and safety. During the discussion, several additional issues, that went beyond this narrow remit, were raised and discussed. Here, we reflect upon some of these, as we understand that NICE welcomes clarification of issues that arise in this way, even if not part of the original presentation.

1) **One Committee Member suggested that a "moralistic" judgement was being made about people using nicotine.** This criticism has been made previously (22). We have not made any such judgement. Advice on the long term use of nicotine, as with exposure to any substance, should be based on evidence of benefits and harm. Our presentation dealt, specifically, only

with the science, and that, specifically with regard to nicotine, what was stated in the presentation was fact: it is currently not designated a carcinogen; but IARC is currently investigating its role in promoting the spread of cancer, subsequent to accumulating new evidence, as referenced.

2) **A Committee Member asked if there were data related to potential "second-hand exposure" to e-cigarette aerosol.** It was noted that American indoor air hygiene organisations have identified the potential for a build-up of exhaled toxicants in ambient air. The American Industrial Hygiene Association (AIHA) (23), therefore, identifies potential risk to bystanders. However, while noting the validity of the precautionary principle here, given the considerable uncertainty that exists, the AIHA has focused primarily on the right to be free from involuntary exposure to potentially hazardous substances, as follows:

   "If the only individual affected by using e-cigarettes were the vaper, the discussion could end here. That is not, however, the case. Similar to secondhand smoke, the ingredients exhaled by the vaper include nicotine, metals, flavorings, and glycol that accumulate in the ambient air. Recipients of secondhand vapor have not chosen to – many, in fact, have explicitly chosen not to – use e-cigarettes. The exposure to secondhand vapor, just like secondhand smoke, raises issues of involuntary exposure and competing rights. This is even more critical for groups that may be, and probably are, more susceptible to adverse effects of secondhand vapor, including children, pregnant women, and people with already compromised health, some of whom may have limited ability to leave the spaces in which vaping occurs or has occurred."

   It is vitally important to note, further, that *e-cigarette users themselves* have identified and reported such "real world" instances and have warned against indoor public use on health grounds due to their own personal experience (24).

3) **One committee member asked if there was scope for issues related to "Conflict of Interest" to be problematic with electronic cigarettes.** In this context, a Committee Member further asked, totally appropriately, if I was aware, when I cited and quoted the expert toxicological opinion of Dr Robert Combes, that he had previously undertaken work for the tobacco company, British American Tobacco (BAT). I confirmed that I was aware of these papers, and suggested that Dr Combes would likely be open to question directly regarding this important issue. Furthermore, Robert Combes and Michael Balls have very recently been *publically asked* about this issue, and their response is available (25) for all, including NICE, to review. This highlights the substantial scope for "Conflicts of Interest" in the field of electronic cigarettes, an issue which has the potential to impact upon advocates of *both* the Tobacco Harm Reduction and the Precautionary Principle in relation electronic cigarettes when it comes to citation and quotation of research.

In this respect, it is important to note the still unresolved controversy regarding one of the most widely cited papers on the safety of e-cigarettes, which form the basis for the claim that these products "were 95% safer than conventional cigarettes". This paper is cited by Action on Smoking and Health UK, who advocate strongly for the potential for electronic cigarettes in smoking cessation, currently, in their "ASH Briefing" entitled "Electronic cigarettes (also known as vapourisers)" (26) document: Nutt, D.J., et al. Estimating the harms of nicotine-containing products using the MCDA approach. European Addiction Research, 2014; 20(5): 218-225". As has been widely discussed, several of the authors have documented links with the tobacco industry, with, firstly, the editors of the paper conceding:

"The editors are aware that K.F. (Karl Fagerstrom) has connections with a company that is associated with one of the largest tobacco industries in the world (BAT: Nicoventures . . .".
Further, the University of Bath University Tobacco Control Research Group has identified that one of the other co-authors, Riccardo Polosa, has previously worked for the tobacco manufacturer Philip Morris USA (27). Moreover, the Bath Group notes that the company funding the research, Euroswiss Health, is owned by an individual who has received funding from British American Tobacco (28). Indeed, this individual, Dr Delon Human, is named in the Royal College of Physicians "Nicotine without smoke" document (29), where the authors note that his claim that "BAT could become part of the solution to addressing the epidemic of tobacco related disease", in a 2013 British American Tobacco sustainability focus report (30).

Delon Human's companies also have links to several of the other authors, not previously known for their expertise in this area. The authors of the Nutt et al paper claim that "We were informed by EuroSwiss Health (Trélex, Switzerland) that they do not receive funding from any tobacco or e-cigarette manufacturers" (31). However, elsewhere, Professor John Britton has stated that "I share . . . concerns over the funding of the MCDA study which generated the 95% estimate for harm relative to tobacco cigarettes. I was invited to take part in that study and declined for reasons that included uncertainty over this matter" (32). Moreover, there has yet to be any satisfactory disclosure of how EuroSwiss Health is funded, given the lack of visibility of any other activity. The questions asked in the discussion about Conflict of Interest are entirely relevant, and, as stated above, represent an important consideration for all observers.

4) **The presenter was asked about his own clinical management in relation to electronic cigarettes.** He stated, fundamentally, what has already been posted on two highly contrasting scientific "blogs" related to smoking cessation and electronic cigarettes, in September, 2014, reflecting a clinically carefully considered, judicious and evidence based discussion with a patient, on a one-to-one basis:

"I DO refer people to their local Smoking Cessation Services for support with quitting via use of an electronic cigarette, if: they have had multiple

attempts via other evidence-based methods but failed; do not wish to try any more via those methods; and if THEY raise the topic of quitting via an electronic cigarette. I will discuss the current evidence base with them: that there is some evidence that on an individual level at least, these devices can help. I do point out that, to maximise the health benefits, that they do need to fully quit, and point out that "dual use" will reduce those potential benefits i.e. they need to "switch". I inform them that, in my opinion, it is inconceivable that an electronic cigarette is either: more harmful, as harmful or, in fact, probably anything like as harmful, as the combustible cigarette." (33; 34).

To this clinical discussion could be added now opinion that the use of electronic cigarettes may potentially *suppress* the chances of successful cessation (35). However, this does not mean that, on an individual basis, full cessation cannot, and does not, occur.

5) **It was claimed that publication of the World Health Organisation's Statement in September 2014 (36) had halted the use of e- cigarettes as cessation aids in one Stop Smoking Service.** However, on closer inspection, this may be somewhat misleading. Professor Robert West commented in February 2015 that electronic cigarette "popularity among continuing smokers has fallen as they find the devices do not always satisfy their nicotine cravings" (37). Moreover, as revealed in a very well-known electronic cigarette advocacy blog (38), the "Smoking Toolkit Survey" demonstrated that the decline in e-cigarette prevalence use amongst smokers and recent ex-smokers dipped: *in the first half of 2014 i.e. prior to the publication of the aforementioned WHO Report.*

6) **It was claimed that there was some evidence suggesting the superiority of "tank systems" over first generation electronic cigarettes.** This was agreed, citing Hitchman et al (39). However, as was pointed out, that study did not utilise biochemical verification, and the actual number of self-reported "fully quit" responders on this on-line survey was only: n=19. The presentation also noted that users of tank systems had experienced a growing number of in-use explosions (40). Recent detailed reviews of such incidents reveal cases of severe injury, as noted in a recent paper in the New England Medical Journal (41) which NICE may need to consider in relation to any type of recommendation in their Guidelines.

7) **It was argued by one Committee Member that there are multiple examples of recommended treatments in healthcare with limited evidence bases.** It is true that some treatments are undertaken based on custom and practice, as they were adopted before it was expected that new treatments would be evaluated. However, we have moved far beyond that now, and we find it quite remarkable that anyone should suggest that a new treatment should be introduced, now, in such a way. This is especially so given that the limited evaluations that these products have been subjected to have failed to find evidence of effectiveness and/or have raised unresolved safety concerns.

8) **A Committee Member commented that a recent paper** (42) **suggested nicotine delivery from Second and Third Generation E-Cigarettes equal to a conventional cigarette, and improved safety.** Even if the nicotine delivery data is replicated, the authors themselves stated: *"Though currently unanswered,* G3 e-cigarettes *may* be more effective smoking cessation devices due to their cigarette-like nicotine delivery profile*"* (emphasis added). The paper, therefore, adds nothing substantive on quitting efficacy, merely presumption. The paper, further, adds nothing in terms of safety. We knew that e-cigarettes do not produce Carbon Monoxide, *and* that levels of NNAL are lower than in tobacco smoke. Some subjects produced higher levels of NNAL than expected, possibly, the authors postulate, the result of unreported tobacco use, which, again, challenges the validity of self-reported abstinence.

References to other work or publications to support your testimony' (if applicable):

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F.4 Expert testimony 4 – Stop smoking services

Expert testimony to inform NICE guideline development

Section A: Developer to complete	
Name:	Dr Andy McEwen
Role:	Executive Director
Institution/Organisation (where applicable):	National Centre for Smoking Cessation and Training (NCSCT)
Guideline title:	Smoking cessation interventions and services (update of NICE guidelines PH1 2006 and PH10 2008)

Guideline Committee:	PHAC F
Subject of expert testimony:	Stop Smoking Services – 'View from the coal face'
Evidence gaps or uncertainties:	Stop smoking services

Section B: Expert to complete

Summary testimony:

Expert testimony presentation slides and discussion covered:
Budget cuts, Integrated 'lifestyle' services, Commissioning, E-cigarettes, Existing NICE recommendations and Q&A.

1. **Budget cuts**

- Some local authorities have decommissioned services entirely, others have no specialist service
- Other services have begun to limit the service they provide for certain groups only (e.g. pregnant women, mental health service users)
- Reduction in the number of staff employed in a number of services has resulted in less, and lower quality, behavioural support received by smokers
- Very few services still have training and CPD budgets and there is a question over the frequency and quality of clinical support and supervision

2. **Integrated 'lifestyle' services**

Brief overview of NCSCT publication:
NCSCT report published August 2016 – titled *Integrated health behaviour (lifestyle) services: a review of the evidence* author Lion Shahab; Editor: Andy McEwen; Reviewers: Jo Locker, Russ Moody, Susan Michie, Robert West copyright National Centre for Smoking Cessation and Training (NCSCT), August 2016. Main findings: The NCSCT reviewed the evidence on integrated services and found no strong argument for their development, quite the contrary, the evidence suggests that smoking should be targeted in isolation.

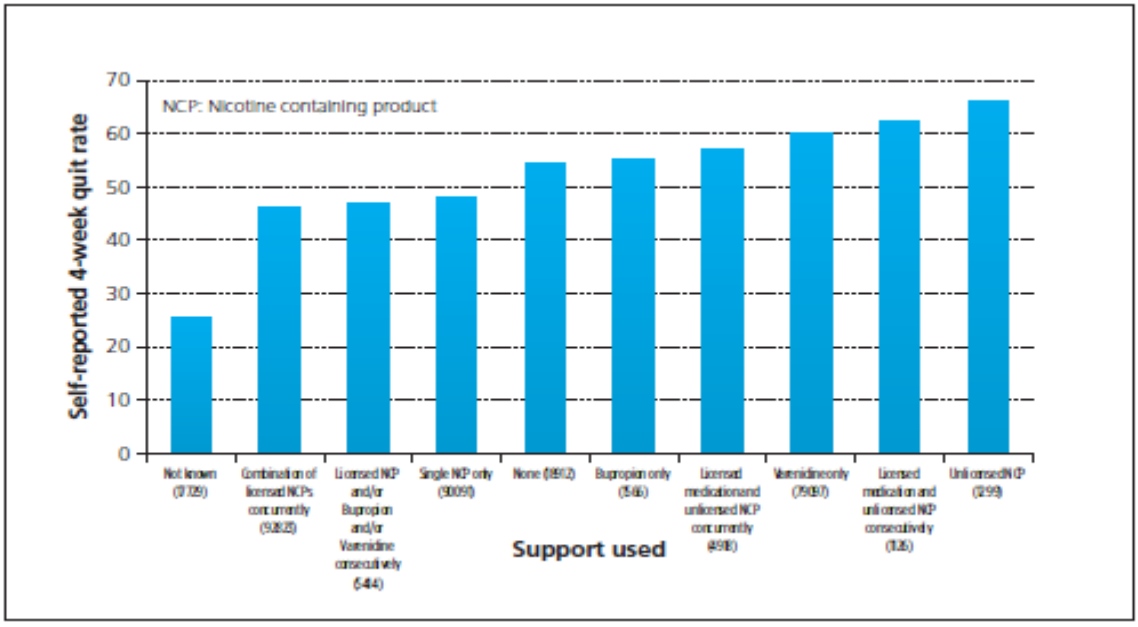
3. **Commissioning**

Brief overview of NCSCT publication:
Local stop smoking services: Service and delivery guidance 2014 NCSCT & Public Health England. ISBN 978-0-9565243-3-1
[*This document also refers to existing recommendations in NICE guidance, PH10 the subject of this update*]. There exists guidance on what services to commission to deliver good quality interventions to smokers, but on the whole these are not being followed.

4. **E-cigarettes**

Brief overview of NCSCT publication:
Electronic cigarettes: A briefing for stop smoking services NCSCT 2016. Authors Andy McEwen and Hayden McRobbie. Reviewers: Jamie Brown, Lynne Dawkins, Peter Hajek, Wayne Hall, Sarah Jakes, Lorien Jollye, Joanne Locker, Louise Ross, Robert West. Produced in Partnership with Public Health England. Version 2. Date of last modification January 2016. ISBN 978-0-9565243-4-8

Figure 2: Four-week self-reported quit rates from English stop smoking services 2014–15[5]



Based on a large number of people still accessing stop smoking services, and the current popularity of e-cigarettes as an aid to quitting, there is an opportunity to improve success rates by combining the most popular (e-cigarettes) with the most effective method of quitting (behavioural support from services).

"An e-cigarette friendly stop smoking service supports clients who want to use an e-cigarette to help them quit smoking and reaches out to smokers considering using an e-cigarette to come to the service for behavioural support."

5. Existing NICE recommendations

[PH10] 1.1.1 *Set realistic performance targets for both the number of people using the stop smoking service and the proportion who successfully quit smoking. These targets should reflect the demographics of the local population.*

Services should aim:

· *to treat at least 5% of the estimated local population who smoke each year*

· *for a successful quit rate of at least 35% at 4 weeks (base this figure on everyone who starts treatment and define success as not having smoked in the third and fourth week after the quit date).* ***[PH10, 2008]***

[PH10] 1.1.2 *Services should validate quit attempts using carbon monoxide monitoring and should defined success as a reading of less than 10ppm at 4 weeks. This does not imply that treatment should stop at 4 weeks.* ***[PH10, 2008]***

[PH10] 1.1.3 *Audit performance data routinely and independently and make the results publicly available. Audit exceptional results (for example, 4-week quit rates lower than 35% or above 70%) to determine the reasons for unusual performance, to help identify best practice and to ensure it is being followed.* ***[PH10, 2006]***

Recommendations 1.1.1, 1.1.2 and 1.1.3, in PH10 are still current.

- Treating 5% of local population who smoke still achievable despite budget cuts, but there is an impact on services with less promotion and marketing.
- 25% LSS independently audited.

- For smokers who start treatment, 50-51% achieve quit rates at 4 weeks. Impressive achievements given the current climate. Morale is low but staff are still committed.
- Smokers are not always aware of a local service and there is still a lack of understanding of what a quality service looks like and Russell standard.
- 60% LSS facing cuts (Ash survey), 40% mid cycle cuts already made, 4 areas have no access to specialist support, 3 areas about to lose specialist support.
- Specialist services replaced with general support from primary care and pharmacy, need to note that behavioural support has a dose response effect, the more you have the better your outcome.
- 5% LSS no specialist support beyond primary care, others focus on treating key groups such as mental health & pregnancy, some provide less person contact, i.e. substitute face to face with telephone contact, shift towards 'lifestyle services' Health behaviour services – healthy eating, weight, stop smoking, alcohol.

6. **Q&A with public health advisory committee**

Discussion covered:
**Pharmacotherapy *Inequality and return on investment *Quality service – what constitutes? *Promote an E-cig friendly service *Involve smokers *Population coverage* *Integrated services – evidence * Behavioural support * Hospital services*

References to other work or publications to support your testimony' (if applicable):

All reports and publications mentioned are available on the NCSCT website
http://www.ncsct.co.uk/

F.5 Expert testimony 5 – Stop-Smoking+

Expert testimony to inform NICE guideline development

Section A: Developer to complete

Name:	Professor Robert West
Role:	Professor of Health Psychology
Institution/Organisation (where applicable):	Health Behaviour Research Centre Department of Epidemiology and Public Health University College London
Guideline title:	Smoking cessation interventions and services (update)
Guideline Committee:	PHAC F
Subject of expert testimony:	Stop-Smoking+: a possible approach to commissioning

Evidence gaps or uncertainties:	Sop smoking services

Section B: Expert to complete

Summary testimony:	[Please use the space below to summarise your testimony in 250–1000 words. Continue over page if necessary]

Summary

The English Stop-Smoking Services (SSS) have been extremely cost-effective and could be more effective if they were all commissioned to follow evidence-based guidance from the National Centre for Smoking Cessation and Training (NCSCT), and the National Institute for Health and Care Excellence (NICE). However, budgetary pressures are leading to downgrading or abandonment of the services in some areas.

The Stop-Smoking+ model is proposed as a possible template that can be used to develop local service delivery plans to maximise the success at stopping smoking that can be obtained with reduced budgets. It is not a substitute for full application of NCSCT and NICE guidance, but a model that may allow Local Authorities to focus reduced resources on support that will be most cost-effective.

The Stop-Smoking+ model consists of presenting smokers (through an online portal, helpline and/or contacts with routine healthcare services) with information about three possible methods of quitting: 1) Specialist Support, 2) Brief Support, and 3) Self-Support. They are told what the method involves, what is required of them, and what the benefits are. They are then provided with easy routes to each of the options.

1. **Specialist Support** involves providing behavioural support and stop-smoking medicines (primarily varenicline or dual form NRT – see below) *fully* in accordance with guidance from the NCSCT and NICE.
2. **Brief Support** involves providing a prescription or voucher for: a) varenicline (Champix), or b) dual form nicotine replacement therapy (NRT) - consisting of transdermal patch plus a faster acting product and advice on use plus a follow-up[2].
3. **Self-Support** involves advice on ways of improving success rates, including advice on e-cigarettes, and links to digital resources.

Details of implementation of the Stop-Smoking+ model will vary according to local needs and resources. The costs will vary according to detailed implementation but would be expected on average to amount to approximately £550,000 for an average Local Authority, including infrastructure and medicines. Applied nationally the Stop-Smoking+ model could generate approximately additional 62,000 long-term ex-smoker each year compared with no support being provided.

Introduction

[2] This is not the same as brief opportunistic advice on smoking which has the primary aim of triggering quit attempts.

Through its National Health Service, England has been at the forefront globally of free provision of evidence-based support for smoking cessation (1). The model has been that any smoker in the country could ask for, and receive, behavioural support and a stop-smoking medicine when they decide to try to quit (2).

As originally conceived the behavioural support was based on face-to-face, group-based or individual sessions conducted by specially trained practitioners weekly, from one or two weeks prior to the target quit date to at least 4 weeks afterwards (3, 4). The stop-smoking medicine on offer was nicotine replacement therapy (NRT), with bupropion (Zyban) and then varenicline (Champix) becoming available in 2000 and 2007 respectively. When delivered to specification this combination of behavioural support and stop-smoking medicines has been found to increase smokers' chances of smoking cessation by around 300 percent compared with what would have happened if they had attempted to stop without any support (5).

In the original vision, this support would be available to any smoker who wanted it. Smokers who did not want to attend behavioural support sessions could be prescribed one of the stop-smoking medicines by their GP (6). This would not be as effective, but could be attractive to more smokers. It was not expected that more than a small proportion of smokers would want to use this service in any one year, but for those who did, it would be a highly cost-effective life-preserving service.

In practice the model that has evolved in England has involved: 1) wide variation in the quality of support offered between different local areas, leading to widely varying performance, and 2) an attempt to ensure that all smokers who receive a stop-smoking medicine also receive behavioural support, usually by staff with less training and supervision than those in the specialist services.

The English Stop-Smoking Services (SSS) have provided support for some 8 million quit attempts since 2000 (7), and at their peak around 2011-2012 they helped an estimated 22,000 smokers each year to stop long term who would not have stopped if they had only used a stop-smoking medicine, thus saving an estimated 24,000 years of life (1). Given the savings to the NHS and wider society when smokers stop, the services will have saved more money than they cost (8). In terms of the scale of lives saved and the return on investment in health and economic terms, the SSS have been among the most significant success stories of the NHS this century.

There was still clear room for improvement. In 2009, The National Centre for Smoking Cessation and Training (NCSCT) was established with central government funding to create a 'virtuous spiral': establishing optimum behavioural support and medication configurations; helping the SSS to implement these, primarily via an online training and assessment programme; and evaluating the results, thus promoting continuing improvements in success rates. An evaluation of the first three years of operation of the NCSCT suggested that it had started to make an impact, particularly in the less well-performing areas (9).

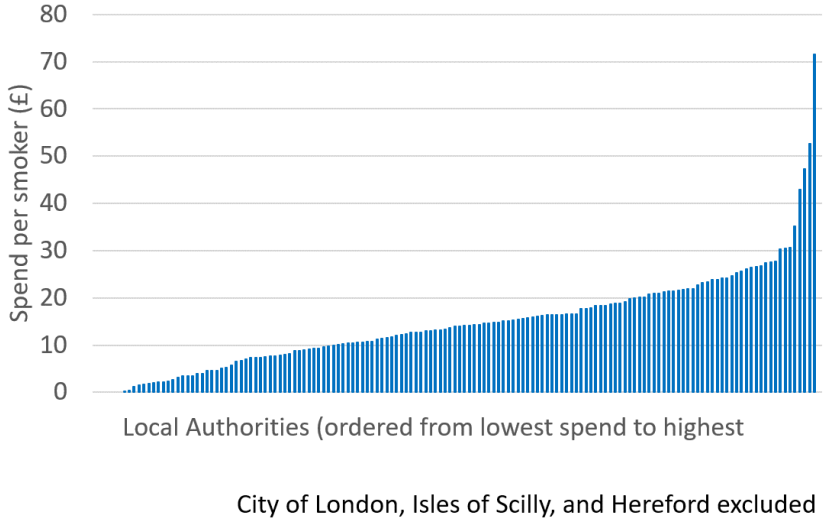
Transferring funding responsibility from the NHS to Local Authorities (LAs) at a time when these authorities are facing unprecedented cuts in central government funding has changed this picture. This has occurred at the same time as substantially increased pressure on NHS resources and personnel. There have also been major reductions in government spending on mass media campaigns. A fourth significant development has been the rapid growth in use of electronic cigarettes (e-cigarettes) for smoking cessation (10).

The changing landscape has meant that the resources available for stop-smoking support have been substantially reduced and some service commissioners are considering whether the services are needed; some specialist services have been cut altogether and many have been incorporated into broader 'lifestyle' services addressing diet, exercise and alcohol consumption (for which evidence on effectiveness and cost-effectiveness is very limited).

Figure 1 shows the amount per smoker in the local population budgeted by each Local Authority for Stop-Smoking Services for 2016-17. It is based on the budgets set (11), their estimated local population aged 16+ (12), and the estimated smoking prevalence in their local population (13). These figures may not always reflect actual expenditure, and some Local Authorities appear to report at least some of the stop-smoking service budgets in a Tobacco Control budget. However, this is unlikely to make a substantial difference to the figures. Another complication is that the cost of stop-smoking medicines is borne to differing degree by Local Authorities and local Clinical Commissioning Groups within the NHS. This means that the overall figure for expenditure is somewhat lower than the true figure when one takes NHS expenditure into account.

The data show that the total Local Authority expenditure budgeted was £105 million (11). The average Local Authority budget for smoking cessation was £686,000 and the average budgeted expenditure per smoker for the country as a whole was £14.58. Figure 1 shows that the amount budgeted per smoker in the population[3] varied considerably from nothing to £70.

Figure 1: Local Authority budgeted spend per smoker in the population for 2016/17



City of London, Isles of Scilly, and Hereford excluded

The level of expenditure overall remains substantial. The problem is that a large number of Local Authorities are spending substantially below this level and some are spending nothing at all. This requires a re-evaluation of the model of stop-smoking support that should be recommended nationally. The Stop-Smoking+ is aimed at providing a template that could be used by commissioners as basis for designing their stop-smoking provision. Each local area will have its own resource and contextual constraints that will influence what is implemented, but the idea of a three tier system from which smokers can choose one that meets their needs could form a useful basis for service development.

[3] Not smoker using the stop-smoking service.

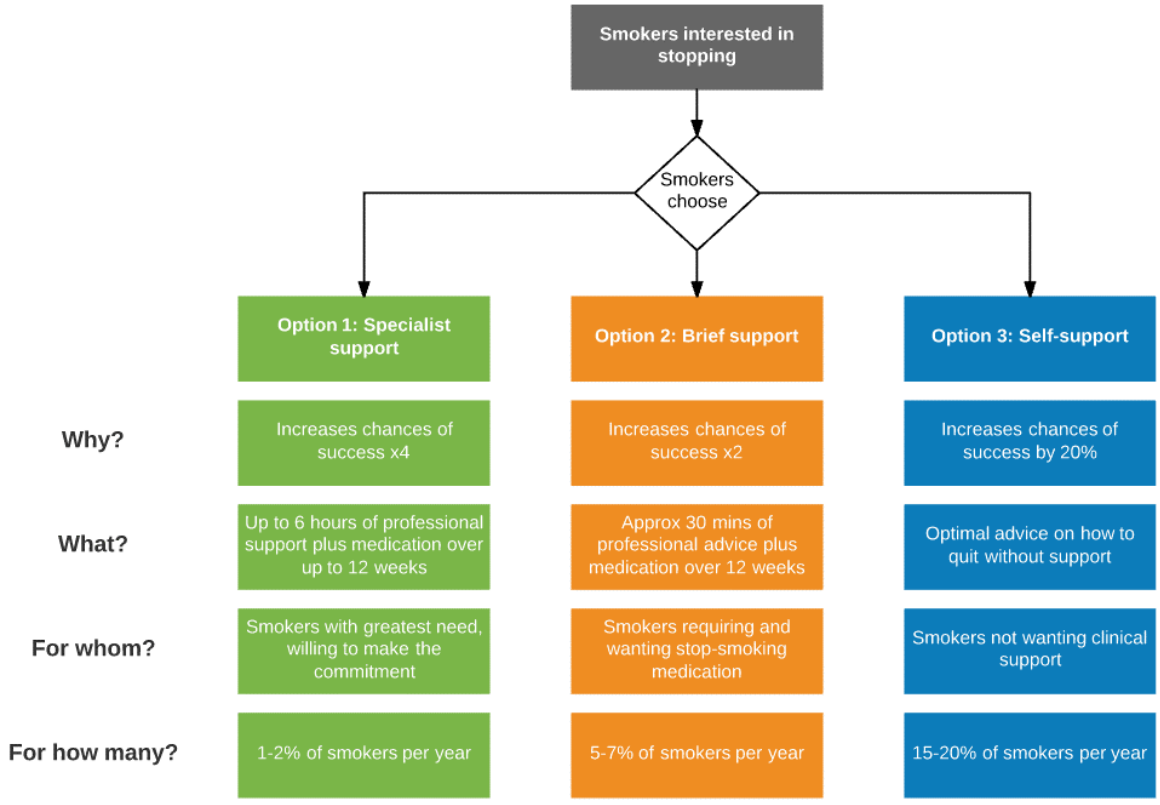
Stop-Smoking+

The model

Stop-Smoking+ (Figure 2) is a model of support that is designed to be applicable locally or regionally to achieve the highest population-level level smoking cessation success rates with limited resources. It has three key features:

1. It places smokers' choice at the heart of the process of determining what method of stopping to use.
2. It involves ensuring that smokers' have the information they need to make their choice in terms of: what the method involves, what it will require of them and what the benefits will be.
3. It focuses on three methods of stopping: 1) Specialist Support, 2) Brief Support, and 3) Self-Support, thereby covering the full spectrum of support to cater for all smokers' needs and preferences.

Figure 2: The Stop-Smoking+ model



Stop-Smoking+ draws on the experience of 18 years of stop-smoking services, and accumulating research into optimal methods of stopping smoking in recognising that:

1. for any given quit attempt only a small proportion of smokers are willing to make the commitment to attend behavioural support sessions, a larger proportion are willing to use a stop smoking medicine, and most smokers want to stop without professional involvement (14).
2. when behavioural support is provided by trained specialist practitioners using the most up-to-date research, success rates can match or exceed those typically found in clinical trials (15).

3. with the resources available it is not realistic to train and supervise healthcare professionals to provide high quality Specialist Support when this is not their primary role.
4. when behavioural support is provided by healthcare professionals to a standard below that set out in NICE and NCSCT guidance documents, success rates are little or no higher than if the smokers had been prescribed a stop-smoking medicine and with brief instructions on use (16).
5. there is emerging evidence that can be conveyed to smokers that will improve their chances of success with Self-Support. This includes advice on abrupt versus gradual quitting (17), use of websites and mobile applications (18), optimal use of licensed nicotine products and use of electronic cigarettes (19-22).

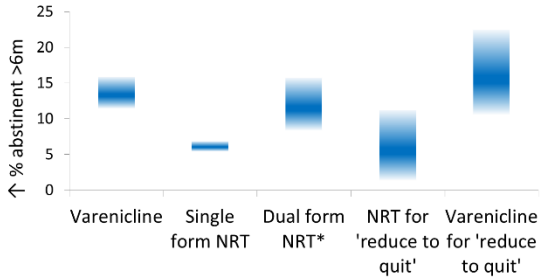
It should be noted that the key cost saving arises from the Brief Support tier where the cost is reduced to little more than the cost of the medication. This is in recognition that the benefits of additional behavioural support that falls short of the full specialist model is minimal on average (see below).

Effectiveness

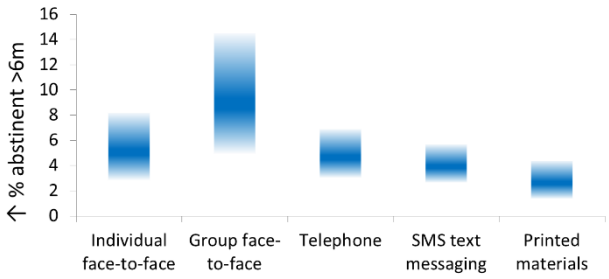
Figures 3a and 3b show estimates derived from Cochrane reviews of effect sizes of components that may go into the different options, while Figure 4 shows estimates of how this would translate into effect sizes for the three options as a whole.

Figure 3: Effectiveness of components of smoking cessation interventions

a) Smoking cessation medicines

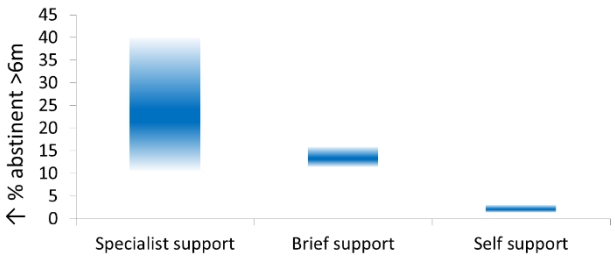


b) Behavioural support options



Note: Estimated percentage point increase in abstinence rates for at least 6 months compared with placebo in the case of stop-smoking medicines, brief advice in the case of face-to-face support, minimal support in the case of telephone counselling and generic materials or nothing in the case of text-messaging and printed materials. Figures for internet interventions and e-cigarettes are not provided as data are not yet sufficiently robust and consistent to provide general estimates. Shaded bars represent 95% confidence intervals for estimates of the average effect size. Data are derived from Cochrane reviews, using percetnage differences in success rates rather than rate ratios (23-31). *Dual form NRT estimate is based on combining figures for dual form versus single NRT and single NRT versus placebo.

Figure 4: Estimates of effectiveness of options in Stop-Smoking+



Note: Estimated percentage point increase in abstinence rates for at least 6 months compared with unaided quitting. Figures are based on combining estimates of effectiveness of components. Shaded bars represent

95% confidence intervals under the assumption of additivity of intervention components. For Self-Support the estimate is based on estimates from using printed materials but no other form of support. If the Self-Support option leads smokers to buy e-cigarettes or engage with other effective methods at their own expense the effect may be higher.

There is an issue concerning the estimation of the additional benefit of specialist behavioural support on top of the effect of medication. Evidence from RCTs indicates that there is a benefit but that it may not be additive as has been assumed in Figure 4. It is extremely important to appreciate, however, that evaluations of behavioural support mostly do not compare it with no support. Instead the intensity of the comparator typically is greater, the greater the intensity of the behavioural support being evaluated (de Bruin, personal communication). This means that the benefit of behavioural support estimated in the Cochrane review is likely to be underestimated. Comparative observational studies with good statistical control for confounding also support the view that more intensive specialist support that is delivered by specialists and include specific behaviour change techniques is more effective than less intensive support provided by healthcare professionals as a small part of their role or not using specific behaviour change techniques (15, 32, 33).

Costs

The cost of implementing the Stop-Smoking+ model depends on the numbers of smokers using each part of the service. The major cost saving compared with previous SSS provision comes from the Brief Support component in which the focus is on ensuring that smokers receive and use stop-smoking medicines; multi-session behavioural support is limited to the smaller proportion of smokers who need it and are willing to commit to attending the sessions.

Table 1 shows indicative costs of the model, but these can be expected to vary with locality and specific implementation.

Table 1: Indicative costs of the Stop-Smoking+ model

	England	**'Average sized' Local Authority**
Number of smokers	8,000,000	53,000
Total cost of Specialist Support[1]	£16,800,000	£112,000
Total cost of Brief Support[1]	£43,200,000	£288,000
Total cost of Self-Support[2]	£12,000,000	£80,000
Total cost of service	*£72,000,000*	*£480,000*
Total ex-smokers[3] created by Specialist Support	9,600	64
Total ex-smokers created by Brief Support[3]	28,800	192
Total ex-smokers created by Self support[3]	24,000	160
Total ex-smokers generated[3]	*62,400*	*416*

[1] Includes infrastructure, training, supervision and medicines, [2] Includes creating and maintain internet-based resources, [3] >6 months continuous abstinence. Full breakdown of costs and effectiveness estimates are available as an Excel spreadsheet from http://www.smokinginengland.info/sts-documents/.

Implementation

The details of implementation of the Stop-Smoking+ model will need to vary according to resources, need and context. The following are important areas for consideration.

1. The strongest evidence is for specialist behavioural support to be provided face-to-face according to the guidance developed by the NCSCT for Public Health England (34), with groups achieving higher success rates at potentially lower unit cost than individual sessions. However, there may be circumstances in which this support has to be provided by telephone. This presents challenges in terms of access to medicines and ability to verify claims of abstinence.
2. There is growing interest in developing bespoke websites and mobile applications to support smokers to stop. This can legitimately be considered part of the Self-Support component, but the evidence base for these aids is not sufficient to consider these as an alternative to Specialist Support or Brief Support (18).
3. There is strong evidence that varenicline or dual form NRT (transdermal patch plus a faster acting product) give the highest success rates and should always be offered or recommended rather than single form NRT (5).
4. A potentially cost-effective way of engaging smokers with Stop-Smoking+ is to construct an online portal that can provide them with the information they require and transfer them quickly and easily to whatever option they select. Figure 5 provides a mock-up of the splash page for such a portal.

Caveats and monitoring

Even with so much evidence on smoking cessation, there is always going to be uncertainty about the effectiveness of different methods in practice. Specific contextual factors can substantially affect the effectiveness of different approaches. In addition, costings are not fixed but can vary depending on the kind of deal one can make with suppliers. Therefore, the figures used in this evidence should be considered indicative and re-evaluated for each local area.

Because of the uncertainties inherent in such a complex behaviour change intervention, independent monitoring of outcomes is crucial and should be built into any commissioning. This should involve continual direct access on behalf of the commissioners to an independent monitoring agent to anonymised data, and audit of claimed success rates using the NCSCT-PHE audit model (35).

Figure 5: Mock-up of the splash page for an online portal for Stop-Smoking+

Conclusions

Stop-Smoking+ has been born out of a need for a broad model of smoking cessation support that makes maximum use of restricted funds. Where Local Authorities are able to sustain levels of funding for smoking cessation support at historic levels, this will save the most lives and save more money to the health service and local economy than is spent on the services. However, where funds are being reduced it is important to ensure that the remaining funds are spent to maximum effect. The Stop-Smoking+ model provides a broad model for achieving that. The detailed implementation will be subject to local circumstances in terms of resources and need.

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Expert testimony and recommendations

Expert testimony	Gaps addressed	Recommendations supported
Latest Cochrane evidence evaluating the safety and effect of using electronic cigarettes for smoking cessation	Data on effectiveness of licensed e-cigarettes (this review was subsequently published and included in this update)	Research recommendation 2
The role of electronic cigarettes in smoking cessation	Advice on e-cigarettes	1.2.6, 1.3.8, 1.3.9
The role of electronic cigarettes in smoking cessation	Advice on e-cigarettes	1.2.6, 1.3.8, 1.3.9
Stop Smoking Services – 'View from the coal face'	Stop smoking services	1.1.1, 1.1.2, 1.1.3, 1.1.4, 1.1.5, 1.1.6, 1.1.7
Stop-Smoking+: a possible approach to commissioning	Stop smoking services	1.1.1, 1.1.2, 1.1.3, 1.1.4, 1.1.5, 1.1.6, 1.1.7

Appendix G: Quality Assessment Tools

G.1 Quality assessment tool for systematic reviews

Adapted from the AMSTAR tool

*quality rating [++] is often described as high quality, [+] as moderate quality and [-] as low quality

Quality Assessment

Item	Decision	Comments
1. Was an 'a priori' design provided? *The research question and inclusion criteria should be established before the conduct of the review.*		
2. Was there duplicate study selection and data extraction?		
3. Was a comprehensive literature search performed?		
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion? *(Grey literature is literature produced at all levels of government, academia, business and industry in print and electronic formats, but is not controlled by commercial publishers. Examples can be but not limited to dissertations, conference proceedings.)*		
5. Was a list of studies (included and excluded) provided?		
6. Were the characteristics of the included studies provided?		
7. Was the scientific quality of the included studies assessed and documented?		
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?		
9. Were the methods used to combine the findings of studies appropriate?		
10. Was the likelihood of publication bias assessed?		

11. Was the conflict of interest included?		
Please describe any other issues that affect the quality of the study and whether this affects the final study quality score.		

G.2 Quality assessment tool for individual studies

QA EPOC Checklist for RCTs, non-randomised controlled trials and controlled before-after studies: draft

Item	Decision	Comments
1. Was the allocation sequence adequately generated?		
2. Was the allocation adequately concealed?		
3. Were baseline outcome measurements similar?		
4. Were baseline characteristics similar?		
5. Were incomplete outcome data adequately addressed?		
6. Was knowledge of the allocated interventions adequately prevented during the study?		
7. Was the study adequately protected against contamination?		
8. Was the study free from selective outcome reporting?		
9. Was the study free from other risks of bias?		.

Appendix H: Quality Assessment Appraisal

H.1 Very brief advice

No evidence identified.

H.2 Brief advice

AUTHOR (YEAR)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	RATING
Rice (2013)	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't answer	Yes	++
Stead(2013)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	++

H.3 Behavioural support

AUTHOR (YEAR)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	RATING
Cahill (2010)	Can't answer	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++
Carr (2012)	Yes	Yes	Yes	Can't answer	Yes	Yes	Yes	No	Yes	No	Yes	+
Huibers(2007)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	No	++
Lancaster (2017)	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	+
Lindson-Hawley (2015)	Can't answer	Yes	Yes	Can't answer	Yes	Yes	Yes	Yes	Can't answer	Yes	Yes	+
Mdege (2014)	Yes	Yes	Yes	Can’t answer	Yes	Yes	Yes	Yes	Yes	No	No	++
Rice (2013)	No	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Can't answer	Yes	++
Stanton(2013)	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Can't answer	No	No	++
Stead(2013)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	No	++

Stead and Lancaster (2017)(Group therapy)	Yes	Yes	Yes	Can't answer	Yes	Yes	Yes	Can't answer	Yes	No	No	++

H.4 Pharmacotherapy with or without behavioural support

H.4.1 Pharmacotherapy alone

AUTHOR (YEAR)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	RATING
Hughes (2014)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++
Stead et al (2012)NRT	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++

H.4.2 Pharmacotherapy with behavioural support

AUTHOR (YEAR)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	RATING
Hughes (2014)	Yes	No	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++
Lancaster (2017)(Individual counselling)	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	No	Yes	+
Mdege (2014)	Yes	Yes	Yes	Can’t answer	Yes	Yes	Yes	Yes	Yes	No	No	++
Stead & Lancaster (2016)	Yes	Can't answer	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++
Stead (2015)	Yes	No	Yes	Can't answer	Yes	Yes	Yes	Yes	Yes	Yes	Yes	++

H.5 Digital media

H.5.1 Individual studies

Japuntich et al 2006

Section 1 Population	the study has been designed or conducted in such a way as to minimise the RoB	Rating
1.1 Is the source population or source area well described?	*Yes*	++
1.2 Is the eligible population or area representative of the source population or area?	*Yes, majority of thsose motivated to quit took part*	++
1.3 Do the selected participants or areas represent the eligible population or area?	*Yes*	++
Section 2. Method of allocation to intervention (or comparison)		++
2.1 Allocation to intervention (or comparison). How was selection bias minimised?	*stated as randomised but method used not reported*	++
2.2 Were interventions (and comparisons) well described and appropriate?	*Yes*	++
2.3 Was the allocation concealed?	*No*	+
2.4 Were participants or investigators blind to exposure and comparison?	*NA as priority outcome'quitting' was biochemically verified*	++
2.5 Was the exposure to the intervention and comparison adequate?	*Yes*	++
2.6 Was contamination acceptably low?	*Yes*	++
2.7 Were other interventions similar in both groups?	Yes	++
2.8 Were all participants accounted for at study conclusion?	Yes	++
2.9 Did the setting reflect usual UK practice?	*Yes*	++
2.10 Did the intervention or control comparison reflect usual UK practice?	Yes	++
Section 3. Outcomes		
3.1 Were outcome measures reliable?	*Yes, biochemically verified quit rate*	++
3.2 Were all outcome measurement complete?	Yes	++
3.3 Were all important outcomes assessed?	yes	++
3.4 Were outcomes relevant?	*Yes*	++

3.5 Were there similar follow-up times in exposure and comparison groups?	*Yes*	++
3.6 Was follow-up time meaningful?	*Yes*	++
Section 4. Analyses		
4.1 Were exposure and comparison groups similar at baseline? If not were these adjusted?	*NA*	++
4.2 Was intention to treat (ITT) analysis conducted?	*Yes*	++
4.3 Was the study sufficiently powered to detect an intervention effect (if one exists)?	*Not reported*	-
4.4 Were estimates of effect size given or calculable?	*Yes*	++
4.5 Were the analytical methods appropriate?	*Yes No identified confounding factors - the statsitical analysis appears apporpriate with rationale clearly stated. In line with other studies in the area*	++
4.6 Was the precision of intervention effects given or calculable? Were they meaningful?	*Not reported*	-
Section 5. Summary		
5.1 Are the study results internally valid (i.e. unbiased)?	Yes	++
5.2 Are the finding generalisable to the source population (i.e. externally valid)?	Yes	++
OVERALL RATING	ALL or MOST of the checklist criteria have been fulfilled	+

Naughton et al 2014

Section 1 Population	the study has been designed or conducted in such a way as to minimise the RoB	Rating
1.1 Is the source population or source area well described?	*UK, Primary care setting, RCT*	++
1.2 Is the eligible population or area representative of the source population or area?	*Well described - Primary care setting - blinding and random allocation in line with methods to reduce potential selection bias*	++
1.3 Do the selected participants or areas represent the eligible population or area?	*Well described; 77.6% invited took up study (n=602) with n=2 withdrawing from intervention arm at allocation stage*	++
Section 2. Method of allocation to intervention (or comparison)		
2.1 Allocation to intervention (or comparison). How was selection bias minimised?	*Randomization was stratified by SCA. The allocation sequence was generated by a computer-based random number generator using random permuted blocks with block sizes of four and six, stored on a remote web server. The sequence was accessible to the*	++

	investigators, who had no involvement in recruitment at participating sites. The sequence was not accessible to the SCAs or participants. Allocation was made by the web server during the consultation once Part 1 of the iQuit questionnaire was submitted (see Procedure). At this point, the SCA and the participant were unblinded to allocation	
2.2 Were interventions (and comparisons) well described and appropriate?	*Yes*	++
2.3 Was the allocation concealed?	*Randomization was stratified by SCA. The allocation sequence was generated by a computer-based random number generator using random permuted blocks with block sizes of four and six, stored on a remote web server. The sequence was accessible to the investigators, who had no involvement in recruitment at participating sites. The sequence was not accessible to the SCAs or participants. Allocation was made by the web server during the consultation once Part 1 of the iQuit questionnaire was submitted (see Procedure). At this point, the SCA and the participant were unblinded to allocation*	++
2.4 Were participants or investigators blind to exposure and comparison?	*Once part 1 of the iQuit questionnaire was completed, the participant was randomized by the online program either to the control group and asked no further questions or to the intervention group and asked a second set of questions (part 2),*	++
2.5 Was the exposure to the intervention and comparison adequate?	*Randomization was stratified by SCA. The allocation sequence was generated by a computer-based random number generator using random permuted blocks with block sizes of four and six, stored on a remote web server. The sequence was accessible to the investigators, who had no involvement in recruitment at participating sites. The sequence was not accessible to the SCAs or participants. Allocation was made by the web server during the consultation once Part 1 of the iQuit questionnaire was submitted (see Procedure). At this point, the SCA and the participant were unblinded to allocation. n=299 (control) and n = 303 (intervention) - drop out less than 1% across both arms the study was powered on point prevalence abstinence for 2 weeks at the 8-week follow-up. A sample size of 300*	++

	per group would give 80% power to detect an increase in abstinence from 20 to 30% (alpha = 0.05, two-sided test),	
2.6 Was contamination acceptably low?	*Yes No evidence of contamination?*	++
2.7 Were other interventions similar in both groups?	Yes	++
2.8 Were all participants accounted for at study conclusion?	Yes	++
2.9 Did the setting reflect usual UK practice?	*UK based study; Primary care; Smoking cessation intervention*	++
2.10 Did the intervention or control comparison reflect usual UK practice?	Yes	
Section 3. Outcomes		
3.1 Were outcome measures reliable?	*Outcomes in line with that expected from smoking cessation - 1) acceptability of service (subjective): 2) Feasability - smokers per practice recruited, response rates to follow-up questionnaire, time taken to complete online questionnaire, increase in length of consultation; particpant perceptions of ease of questionnaire completion 3) utilisation of biomedical and service standards for the mesurement - the study highlights some deviation from the Russell standard but this was underpin but what appears to be a firm rationale.*	++
3.2 Were all outcome measurement complete?	Yes	++
3.3 Were all important outcomes assessed?	Yes	++
3.4 Were outcomes relevant?	*NA - No surrogate measures*	++
3.5 Were there similar follow-up times in exposure and comparison groups?	*no differences in follow-up across groups*	++
3.6 Was follow-up time meaningful?	*The study flags that the primary role of this study was to investigate the feasability of the intervention for a larger RCT Although there is a relatively short follow up for a behaviour intervention - it does undertake a longer follow-up 6m via telephone/post but they did not undertake CO measures or validate abstinence biochemically*	++
Section 4. Analyses		
4.1 Were exposure and comparison groups similar at baseline? If not were these adjusted?	*No statistical calculation for difference but looking across the table there doesn't appear to be anything massively different in the baseline sample (sex, mean, age etc and mean cigarette consumption etc - see Table 1)*	++

4.2 Was intention to treat (ITT) analysis conducted?	*The smoking outcome analyses were intention-to-treat, where all those randomized were analysed with participants lost to follow-up assumed to be smoking. We also conducted sensitivity analyses using a range of less severe assumptions, namely a complete-case analysis and relaxation of the 4-week abstinence definition*	++
4.3 Was the study sufficiently powered to detect an intervention effect (if one exists)?	*the study was powered on point prevalence abstinence for 2 weeks at the 8-week follow-up. A sample size of 300 per group would give 80% power to detect an increase in abstinence from 20 to 30% (alpha = 0.05, two-sided test), informed by a systematic review showing a relative increase in abstinence among smokers receiving tailored materials versus no materials of 40% at 6 months*	++
4.4 Were estimates of effect size given or calculable?	*Yes - no effect on smoking outcomes between groups: 1) 2-week point prevalence abstinence at the 8-week primary end-point [control 40.3%, iQuit 45.2%; odds ratio (OR) = 1.22, 95% CI = 0.88–1.69] or in any secondary short-term abstinence outcomes 2) Statistically significant group differences were found for 6-month prolonged abstinence at 6 months (control 8.9%, iQuit 15.1%; OR = 1.81, 95% CI = 1.09–3.01) and for 6-month continuous abstinence (control 6.3%, iQuit 11.4%; OR = 1.92, 95% CI = 1.07–3.45).*	++
4.5 Were the analytical methods appropriate?	*No identified confounding factors - the statsitical analysis appears apporpriate with rationale clearly stated. In line with other studies in the area*	++
4.6 Was the precision of intervention effects given or calculable? Were they meaningful?	*CI appear narrow and indicate adquate precision; study adequatly powered*	++
Section 5. Summary		
5.1 Are the study results internally valid (i.e. unbiased)?	Yes	++
5.2 Are the finding generalisable to the source population (i.e. externally valid)?	Yes	++
OVERALL RATING	++ ALL or MOST of the checklist criteria have been fulfilled	++

Pakhale et al 2015

Section 1 Population	the study has been designed or conducted in such a way as to minimise the RoB	Rating

1.1 Is the source population or source area well described?	*Canada - Adult tobacco smokers attending the respirology clinic and willing to choose a quit date within one month of enrollment were randomly assigned to receive standard care or the intervention.*	++
1.2 Is the eligible population or area representative of the source population or area?	*This is a pilot study: The clinic team identified smokers and were asked to complete a screening eligibility form by a clinic nurse or a research team member. This form included smoking-related questions (smoking in past seven days, years smoked, amount smoked daily, confidence in and importance of quitting, number of quit attempts in the past year). Those who met the eligibility criteria and were interested were given more information and invited to sign a consent form*	++
1.3 Do the selected participants or areas represent the eligible population or area?	*a pilot study: 54.4% of those identified were randomised (49/90)*	+
Section 2. Method of allocation to intervention (or comparison)		
2.1 Allocation to intervention (or comparison). How was selection bias minimised?	*identified smokers and were asked to complete a screening eligibility form Randomization performed immediately after enrollment. Sealed and opaque envelopes were prepared by UOHI using a computer-generated allocation sequence based on stratified (according to sex) block randomization. Those responsible for randomization were unaware of upcoming group assignments. Blinding of participants was not possible due to the nature of the intervention*	++
2.2 Were interventions (and comparisons) well described and appropriate?	Yes	++
2.3 Was the allocation concealed?	*Randomization was performed immediately after enrollment. Sealed and opaque envelopes were prepared by UOHI using a computer-generated allocation sequence based on stratified (according to sex) block randomization. Those responsible for randomization were unaware of upcoming group assignments. Blinding of participants was not possible due to the nature of the intervention*	++
2.4 Were participants or investigators blind to exposure and comparison?	*Those responsible for randomization were unaware of upcoming group assignments. Blinding of participants was not possible due to the nature of the intervention*	++

2.5 Was the exposure to the intervention and comparison adequate?	*nothing that would indicate bias - small sample and under powered but nothing regarding exposure*	++
2.6 Was contamination acceptably low?	*No indication of contamination*	++
2.7 Were other interventions similar in both groups?	*nothing to indicate that any bias was present in the delivery of the intervention*	++
2.8 Were all participants accounted for at study conclusion?	*yes*	++
2.9 Did the setting reflect usual UK practice?	*Yes - OECD country - similar healthcare set up, delivery or recruitment to study would have occured in a similar way in UK*	++
2.10 Did the intervention or control comparison reflect usual UK practice?	*there is a lack of detail but the intervention details provided don't indicate that this would be a source of bias - and probably reflects UK practice - i.e. smoking specialist deliverying interventions to a population identified in a primary care setting as smokers*	+
Section 3. Outcomes		+
3.1 Were outcome measures reliable?	*Self-reported There is reference to Russell Standard regrading smoking status data which is a an accepted validated measurement scale in this area*	+
3.2 Were all outcome measurement complete?	*yes*	++
3.3 Were all important outcomes assessed?	*There was an absence of biomedical items - but the study did not set out to investigate this. It measured all it set out to in the study methodology.*	++
3.4 Were outcomes relevant?	*no surrfogate measures utilised* *- main smoking measure was self reported smoking status; feasability of the intervention was also a primary outcome and measures directly assessed this*	++
3.5 Were there similar follow-up times in exposure and comparison groups?	*Yes - similar follow-up times*	++
3.6 Was follow-up time meaningful?	*Yes there appears to be a measure of the automated calls up to 180 days post quit date. This appears suitable but no gold standard is mentioned regarding this - ?*	+
Section 4. Analyses		
4.1 Were exposure and comparison groups similar at baseline? If not were these adjusted?	*No statistical measures for difference of baseline charateristics but study narrative outlines "Baseline differences between the*	++

	intervention and control group were nonsignificant"- appears similar a 10% difference in terms of educational level (high school or greater) between control and intervention - all other baseline measures seem 'similar'	
4.2 Was intention to treat (ITT) analysis conducted?	*assume not - not documented in the narrative*	-
4.3 Was the study sufficiently powered to detect an intervention effect (if one exists)?	*No power calculation reported - small sample size so assume under powered - Author also flags this as a limitation. As this is a 'pilot study' does this study need to be adequately powered?*	-
4.4 Were estimates of effect size given or calculable?	*Yes: Self-reported smoking status: 2.36 (95% CI 0.39 to 14.15). Observed differences between groupswere not statistically significant (P=0.654).*	++
4.5 Were the analytical methods appropriate?	*Yes - no differences that required additional adjustments*	++
4.6 Was the precision of intervention effects given or calculable? Were they meaningful?	*Small sample - author flags the study as being under powered. The OR for self-reported nonsmoker status was 2.36 (95% CI 0.39 to 14.15). Observed differences between groups were not statistically significant (P=0.654). CI's relatively wide but this could be explained by the small sample/under powered study.*	++
Section 5. Summary		
5.1 Are the study results internally valid (i.e. unbiased)?	*apart from the sample size the study is well designed*	++
5.2 Are the finding generalisable to the source population (i.e. externally valid)?	+ UNCLEAR or NOT ADDRESSED all potential RoB	+
OVERALL RATING	+ SOME of the checklist criteria have been fulfilled	+

Appendix I: Committee membership and Declarations of interest

I.1 Membership list

Name	Job Title, Organisation
Chair	
Sharon Hopkins	Interim Chief Executive, Cardiff and Vale University Health Board
Vice-chair	
John Macleod	Professor of Clinical Epidemiology and Primary Care, University of Bristol
Core members / Members	
David McDaid	Senior Research Fellow in Health Economics and Health Policy, London School of Economics and Political Science
Stuart Lines	Triborough Consultant in Public Health & Deputy Director of Public Health for L
Rachel Chapman	Public Health Specialty Regsitrar, Health Education West Midlands
Ruairidh Milne	Professorial Fellow in Public Health, University of Southampton
Helene Dyson	Commissioning, Wokingham Borough Council
Charles Penn	Independent Consultant
Derek Ward	Professor of Public Health & Public Health Advisor - Derbyshire CCGs
Chris Weston	Consultant in Public Health
Ann Nevinson	Lay member
Topic expert members	
Deborah Arnott	Chief Executive, Action on Smoking and Health (ASH)
Kamran Siddiqi	Professor in global public health, University of York
Louise Ross	Stop smoking service manager
Sanjay Agrawal	Consultant Respiratory Physician, University Hospitals of Leicester NHS Trust
Rachel Tennant	Specialist New Leaf Advisor, Nottingham CityCare Partnership

Sarah Jakes	Lay member

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I.1 Declarations of Interests

The effective management of conflicts of interests is an essential element in the development of the guidance and advice that NICE publishes. Please refer to the NICE website for the Policy on Conflicts of Interest.

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
Sharon Hopkins	Director of Public Health, Cardiff and Vale University Health Board **(Role upon recruitment June 2015)**	Director of Public Health Cardiff and Vale University Health Board , Wales Fellow of Faculty of Public Health Declarations upon recruitment – June 2015	Non-specific, personal, non-financial	Declare and participate
	Interim Chief Executive, Cardiff and Vale University Health Board (**From 01 December 2016 - 20 July 2017)**	Overall responsibility for population services in the area (Cardiff and Vale) (18 January 2017: Committee meeting)	Non-specific, personal, non-financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
John Macleod	Professor of Clinical Epidemiology and Primary Care, University of Bristol	I work for an academic institution that may undertake research of relevance to NICE Public Health advice	Non-specific, personal, non-financial	Declare and participate
David McDaid	Senior Research Fellow in Health Economics and Health Policy, London School of Economics and Political Science	I do not have any specific conflict of interests related to the topics that have been discussed by the PHAC F Committee. However, as a university researcher I continue to author/co-author a range of academic papers, particularly in the area of mental health promotion, and hold and continue to apply for research grants in the broad area of the economics of health promotion and disease prevention. I have also received speaker honorariums and travel expenses in the last 12 months from the pharmaceutical companies Otsuka and Lundbeck to attend conferences to speak on the economic costs of living with schizophrenia and will receive an honorarium from Janssen-Cilag to speak about the costs of schizophrenia at a conference in October 2015.	Non-specific, personal, financial and non-financial	Declare and participate
Stuart Lines	Triborough Consultant in Public Health & Deputy Director of Public Health for L	None	No interests	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
Rachel Chapman	Public Health Specialty Registrar, Health Education West Midlands	I did some initial exploratory work with Pfizer (contact made through the ABPI) looking at whether they could support our stop smoking services but the project was not progressed. This was more than 12 months ago in a previous role. (30 June 2016: Committee meeting)	Non-specific, non-personal, financial	Declare and participate
	Public Health Specialty Registrar, Health Education West Midlands	Rachel will be carrying out work in relation to smoking in pregnancy (07 September 2016: Committee meeting)	Non-specific, personal, non-financial	Declare and participate
Ruairidh Milne	Professorial Fellow in Public Health, University of Southampton	I am a Fellow of the Faculty of Public Health. (16 June 2015: Recruitment)	Non-specific, personal, non-financial	Declare and participate
	Professorial Fellow in Public Health, University of Southampton	I have an honorary contract as consultant in public health medicine with University Hospital Southampton NHS Foundation Trust. (16 June 2015: Recruitment)	Non-specific, personal, financial	Declare and participate
	Professorial Fellow in Public Health, University of Southampton	I work for NETSCC which will carefully consider all research recommendations in PHAC guidance and may commission independent research to address those recommendations. NETSCC is based in the University of Southampton and it is possible that researchers in the University may bid for or undertake research in the areas covered by this guideline. I am not aware of any current plans along these lines. (16 June 2015: Recruitment)	Non-specific, non-personal, non-financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
	Professorial Fellow in Public Health, University of Southampton	I also have a contract with the UK Cochrane Centre to help teach young doctors about evidence-based practice	Non-specific, personal, financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
Helene Dyson	Commissioning, Wokingham Borough Council	None	No interests	Declare and participate
Charles Penn	Independent Consultant	Shareholding in GSK held by spouse. Shareholding in GW Pharmaceuticals held by self. Each shareholding amounts to less than 1% combined assets (28 June 2015: Recruitment)	Specific, personal, financial	Initial decision that member should declare and participate. On review it was identified that he should not have participated due to GSK manufacture of bupropion. All recommendations were then reviewed with the other committee members separately to confirm their confidence in them.

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
	Independent Consultant	As a founder director of the Health Protection Agency (now Public Health England) spin-out company Syntaxin Ltd I held shares in the company. Syntaxin has now been sold but shareholders may continue to receive further (deferred) consideration based on product development milestones (28 June 2015: Recruitment)	Non-specific, personal, financial	Declare and participate
Derek Ward	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	I am an Academic (3 days per week) who researches in the field of Public Health so there may be an interest to disclose if the PHAC is looking at an area I am researching or applying for funds in (28 June 2015: Recruitment)	Non-specific, personal, non-financial and financial	Declare and participate
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	I am also an employee of Southern Derbyshire Clinical Commissioning Group and, depending on the nature of guidance development, this may also result in an interest. (28 June 2015: Recruitment)	Non-specific, non-personal, non-financial	Declare and participate
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	I am a member of the NICE Local Government Advisory group (28 June 2015: Recruitment)	Non-specific, personal, non-financial	Declare and participate
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	I work for an academic institution that may undertake research of relevance to NICE Public Health advice. My organisation could be involved in research or in making applications for grants related to topics that may be discussed. (12 July 2016: Committee meeting)	Non-specific, non-personal, financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	As an advisor to the 4 Derbyshire Clinical Commissioning Groups I may be asked for professional advice in topics that may be discussed by the committee. (12 July 2016: Committee meeting)	Non-specific, personal, non-financial	Declare and participate
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	As a researcher and public health Consultant, I advocate for improvements in health and reduction of health inequalities, including for children. (12 July 2016: Committee meeting)	Non-specific, personal, non-financial	Declare and participate
	Professor of Public Health & Public Health Advisor - Derbyshire CCGs	As a previous Director of Public Health I was responsible for commissioning aspects of smoking cessation services. (12 July 2016: Committee meeting)	Specific, personal, non-financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
Chris Weston	Consultant in Public Health	I am lead commissioner for Lincolnshire's Smoking Cessation service, currently provided by North 51 (Quit 51 in Lincolnshire). Quit 51 provide a range of initiatives in County including telephone support and pharmacotherapy (in conjunction with primary care prescribers) (12 October 2016: Committee meeting)	Specific, personal, non-financial	Declare and participate
Ann Nevinson	Lay member	None	No interests	Declare and participate
Deborah Arnott	Chief Executive, Action on Smoking and Health (ASH)	I am the chief executive of an organisation which advocates for evidence-based measures to reduce smoking prevalence which includes smoking cessation policy. I have no relevant financial interests – neither ASH nor I, nor any member of my family, accept commercial funding from the pharmaceutical industry, the electronic cigarette industry or the tobacco industry. (16 November 2015: Recruitment)	Specific, personal and non-personal, financial & non-financial	Declare and participate
		Author and co-author of the below: Britton J. Arnott D. McNeill A. Hopkinson N. Nicotine without smoke—putting electronic cigarettes in context. BMJ 2016; 353 doi: https://doi.org/10.1136/bmj.i1745 (Published 27 April 2016) Hiscock R, Goniewicz ML, McEwen A, Murray S, Arnott D, Dockrell D and Bauld L. Ecigarettes:	Specific, personal and non-personal, non-financial	Declare and participate

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
		online survey of UK smoking cessation practitioners. Tobacco Induced Diseases 2014 12; 13 Laverty AA, Watt HC, Arnott D, Hopkinson NS. Standardised packaging and tobacco industry-funded research. The Lancet 2014 383; (9926): 1384 Britton J;McNeill A;Arnott D;West R;Godfrey C. Drugs and harm to society. Lancet. 2011. 377(9765):551-551 West R;Mcneill A;Britton J;Bauld L;Raw M;Hajek P;Arnott D;Jarvis M;Stapleton J. Should smokers be offered assistance with stopping?. Addiction. 2010. 105(11):1867-1869 Gilmore AB;Britton J;Arnott D;Ashcroft R;Jarvis MJ. The place for harm reduction and product regulation in UK tobacco control policy. J Public Health (Oxf). 2009. 31(1):3-10 Britton J;McNeill A;Arnott D;West R;Godfrey C. Assessing drug-related harm. Lancet. 2007. 369(9576):1856-1857 Hammond D;Wiebel F;Kozlowski LT;Borland R;Cummings KM;O'Connor RJ;McNeill		

Name	Job title, organisation	Declarations of Interest, date declared	Type of interest	Decision taken
		A;Connolly GN;Arnott D;Fong GT. Revising the machine smoking regime for cigarette emissions: implications for tobacco control policy. Tob Control. 2007. 16(1):8-14 Lewis S;Arnott D;Godfrey C;Britton J. Public health measures to reduce smoking prevalence in the UK: how many lives could be saved?. Tob Control. 2005. 14(4):251-254 **Linda Bauld [1,2,*], AnneMarieMacKintosh [1,2], Brian Eastwood [3], Allison Ford [1,2], GrahamMoore [4], Martin Dockrell [3], Deborah Arnott [5], Hazel Cheeseman [5] and Ann McNeill [2,6]** *Young People's Use of E-Cigarettes across the United Kingdom: Findings from Five Surveys 2015-2017,* International Journal of Environmental Research and Public Health 2017, 14, 29 August 2017 http://www.mdpi.com/1660-4601/14/9/973/pdf Simonavicius E, McNeill A, Arnott D, Brose LS. What factors are associated with current smokers using or stopping e-cigarette use? Drug Alcohol Dependence 2017;173:139-143. doi: 10.1016/j.drugalcdep.2017.01.002. [Epub ahead of print]		

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Kamran Siddiqi	Professor in global public health, University of York	I have an academic interest in smoking cessation. I have secured research income through my University department from NIHR, MRC, EU, IDRC and Pfizer to conduct research in smoking cessation. (17 November 2015: Recruitment)	Specific, personal, non-financial	Declare and participate
Louise Ross	Stop smoking service manager	I have had no personal reward from any industry connected with tobacco, pharmaceutical products or electronic cigarettes. I have written a few articles for journals for which I have received a fee. (19 November 2015: recruitment)	Non-specific, personal, financial	Declare and participate
	Stop smoking service manager	My team (Stop Smoking Service) has received support from pharmaceutical firms in the form of small educational grants, support with training events.	Specific, non-personal, financial	Declare and participate

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Sanjay Agrawal	Consultant Respiratory Physician, University Hospitals of Leicester NHS Trust	I Chair the British Thoracic Society Tobacco advisory group, am a member of the Royal College of Physicians Tobacco advisory group and am a board member for ASH (Action on Smoking for Health) as well as having published editorials and original research in the field of smoking cessation.	Specific, personal, non-financial	Declare and participate
Rachel Tennant	Specialist New Leaf Advisor, Nottingham CityCare Partnership	None (11 June 2016: committee meeting)	No interest	Declare and participate
Sarah Jakes	Lay member	Has participated in television interviews on the topic	Specific, personal, non-financial	Declare and participate

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