Behavioural programmes for cigarette smoking cessation: investigating interactions between behavioural, motivational, and delivery components in a systematic review and component network meta-analysis

Jamie Hartmann-Boyce[1]*

José M Ordóñez-Mena[1][3]

Jonathan Livingstone-Banks[1]

Thomas R Fanshawe[1]

Nicola Lindson[1]

Suzanne C Freeman[2]

Alex J Sutton[2]

Annika Theodoulou[1]

Paul Aveyard[1][3]

[1] Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK

[2] Department of Health Sciences, University of Leicester, Leicester, UK

[3] NIHR Oxford Biomedical Research Centre, Oxford, UK

*Contact person. Jamie.hartmann-boyce@phc.ox.ac.uk. Nuffield Department of Primary Care Health Sciences; University of Oxford; Radcliffe Observatory Quarter; Woodstock Road; Oxford; OX2 6GG; UK

Running head

Behavioural support for smoking cessation: network meta-analysis

Word count 3929

Declarations of interest

None to declare; This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure and Cochrane Programme Grant funding to the Cochrane Tobacco Addiction Group, and via the NIHR Complex Reviews Support Unit (AS and SF). The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service, or the Department of Health and Social Care. PA is an NIHR senior investigator and is funded by NIHR Oxford Biomedical Research Centre (BRC) and the NIHR Collaboration for Leadership in Applied Health Research and Care (CLAHRC) Oxford.

JMOM receive funding from the NIHR BRC, Oxford and the NIHR Applied Research Collaboration (ARC) Oxford and Thames Valley at Oxford Health NHS Foundation Trust.

TF receives funding from the NIHR Community Healthcare MedTech and In Vitro Diagnostics Co-operative at Oxford Health NHS Foundation Trust and the NIHR Applied Research Collaboration Oxford and Thames Valley at Oxford Health NHS Foundation Trust.

ABSTRACT

Aims

To investigate the comparative and combined effectiveness of four types of components of behavioural interventions for cigarette smoking cessation: behavioural (e.g. counselling), motivational (e.g. focus on reasons to quit), delivery mode (e.g. phone), and provider (e.g. nurse).

Design

Systematic review and component network meta-analysis of randomized controlled trials identified from Cochrane reviews. Interventions included behavioural interventions for smoking cessation (including all non-pharmacological interventions, e.g. counselling, exercise, hypnotherapy, self-help materials), compared with another behavioural intervention or no support. Building on a 2021 review (CD013229), we conducted three analyses, investigating: comparative effectiveness of the components, whether models that allowed interactions between components gave different results to models assuming additivity, and predicted effect estimates for combined effects of components that had showed promise but where there were few trials.

Setting

Community and healthcare settings

Participants

Adults who smoke tobacco

Measurements

Smoking cessation at ≥6 months, preferring sustained, biochemically validated outcomes where available.

Findings

312 trials (250,563 participants) were included. 50 were at high risk of bias using Cochrane risk of bias tool, V1 (ROB1); excluding these studies did not change findings. Head-to-head comparisons of components suggested that support via text-message (SMS) compared with telephone (odds ratio (OR) 1.48, 95% credibility interval (CrI) 1.13 to 1.94) or print materials (OR 1.44, 95% CrI 1.14 to 1.83) was more effective, individual delivery was less effective than delivery as part of a group (OR 0.78, 95% CrI 0.64 to 0.95). There was no conclusive evidence of synergistic or antagonistic interactions when combining components that were commonly used together. Adding multiple components that are commonly used in behavioural counselling suggested clinically relevant and statistically conclusive evidence of benefit. Components with the largest effects that could be combined, but rarely have been, were estimated to increase the odds of quitting between two and threefold. For example, financial incentives delivered via SMS, with tailoring a focus on how to quit, had an estimated OR of 2.94 (95% CrI 1.91 to 4.52).

Conclusions

Among the components of behavioural support for smoking cessation, behavioural counselling and guaranteed financial incentives are associated with the greatest success. Incorporating additional components associated with effectiveness may further increase benefit, with delivery via text-message showing particular promise.

Keywords: smoking cessation; behavioural support; counselling; tobacco addiction; systematic review; meta-analysis

INTRODUCTION

Smoking remains a leading cause of preventable morbidity and mortality worldwide.(1) Most people who smoke want to quit, but stopping smoking is challenging and most attempts to quit are unsuccessful, even when using evidence-based stop smoking interventions.(1-3) Smoking cessation can reverse much of the damage caused by tobacco use, particularly at younger ages, and even in those aged greater than 60.(4-7) Therefore, it is important to provide effective support for quit attempts to as many people as possible to improve public health.

Behavioural support is commonly offered to help people quit cigarette smoking, either with or without cessation pharmacotherapies.(8) However, behavioural support varies in behavioural and theoretical content, training of person(s) providing the intervention, and mode(s) of delivery.(9) Previous meta-analyses investigating effectiveness of behavioural support for smoking cessation have compared two conditions – for example telephone counselling versus self-help only (e.g. (10)) – limiting the ability of these reviews to investigate comparative effectiveness between active treatments. By contrast, network meta-analysis is a statistical method for comparing multiple interventions simultaneously in a single analysis, using aggregate data from clinical studies to produce effect estimates informed by both direct and indirect evidence.(11) Whereas traditional pairwise meta-analysis only allows direct comparisons between two interventions (e.g. nicotine replacement therapy versus placebo), network meta-analysis allows multiple comparisons to be calculated simultaneously (for example, network meta-analysis has been used to compare different classes of stop smoking pharmacotherapies to one another, e.g. (2)). Such an approach, however, gets increasingly challenging with complex interventions, including behavioural interventions which consist of many different elements. Component network meta-analysis (CNMA) therefore advances network meta-analysis a step further in order to evaluate comparative effectiveness of different characteristics – or components – of interventions.(12)

We recently completed a Cochrane overview of reviews, incorporating a CNMA of behavioural interventions for smoking cessation.(3)Evidence of benefit was strongest for behavioural counselling and guaranteed financial incentives. Evidence also suggested possible benefit of: individual tailoring; delivery via text message (SMS), email, and audio recording; delivery by lay health advisor; and intervention content with motivational components and a focus on how to quit.

The Cochrane Review presented effect estimates only for individual components estimated in the CNMA, representing the contribution of that component to an intervention when compared with minimal intervention, whereas support typically comprises a set of components (e.g. at least one mode of delivery, one motivational and one behavioural component).

The original review assumes that the component effects (estimated with odds ratios, ORs) obtained in this CNMA (hereafter the 'original model') were multiplicative (additive on the log scale). Therefore, to assess the likely effectiveness of a particular form of behavioural support combining two or more components, one would multiply the ORs (or add them if in the log scale) for each of the components that make up the intervention. However, this would not yield estimates of uncertainty, and assumes no interactions between components.

The original report did not facilitate direct comparisons between components e.g. different providers or methods of delivery. While this could easily be done by taking the ratio between ORs for different components (or subtracting component effects on the log scale), no measure of uncertainty could be easily estimated. Although in theory none of the components are mutually exclusive, in practice, head-to-head comparisons between components such as delivery modes are important when making decisions about service provision.

Therefore, in this paper, we reanalyse the data from the original review. Our aims were to: a) calculate effect estimates and associated uncertainty for direct comparisons between components; b) gain further insight by identifying potential interactions between components; and c) calculate effect estimates for combinations of components, both those currently most commonly delivered, and those which the original model suggested show the most promise, but for which trial data are currently scarce. We specified these particular exploratory analyses in advance, based on their relevance to decisions regarding best use of resource for smoking cessation support. We also focussed on intervention opportunities afforded by new technology, and the continued need to consider *what* is delivered in behavioural smoking cessation programmes, as well as *how* it is delivered.

METHODS

A protocol for the Cochrane overview and CNMA was published in advance and contains full details on searches, screening, inclusion criteria, definition and selection of components, data extraction, and risk of bias assessment methods; a brief description is provided below.(3) An analysis plan for this re-analysis was preregistered; we did not deviate from this plan.(13)

Search and inclusion criteria

This is a secondary analysis and search and inclusion criteria follow those previously set out. (3) In brief, we searched Cochrane reviews (July 2020) for randomized controlled trials of behavioural interventions for smoking cessation that could be provided to the general adult population of people who smoked, with follow-up of at least six months.

Screening, data extraction, and risk of bias assessment

We followed standard Cochrane methods for screening, data extraction, and risk of bias assessment.

The outcome of interest was smoking cessation at six months or longer from baseline, including all participants randomised in their original groups. The preferred measurement of cessation was biochemically validated continuous or prolonged abstinence, measured at the longest reported time point, but less stringent measures were used (e.g. point prevalence, self-report) where this was not available. All participants lost to follow-up were assumed to be smoking, as is standard.(14)

Studies were assessed using the Cochrane risk of bias tool, V1, following standard Cochrane Tobacco Addiction Group.(15) We judged a study to be at low risk of bias overall if all domains were judged to be at low risk of bias. We considered it at high risk if it was judged to be at high risk of bias in one or more domains. We considered all other studies as unclear risk. Components were coded independently and in duplicate, based on a pre-defined framework agreed *a priori* by all members of the study team based on existing literature (e.g. (16)), including clinicians and experts by experience.

Data synthesis

As in the original model, we used Bayesian CNMA models, with adjustment for multi-arm studies, to estimate the effects of components compared with minimal intervention. We defined 36 behavioural and motivational, provider, and delivery components (Table 1). We conducted sensitivity analyses to determine whether results changed after removing studies at high risk of bias.

CNMA models were similar to those used by Freeman and colleagues and adapted to include a binomial likelihood with logit link for binary outcome.(12) Bayesian analyses were run using WinBUGS version 1.4.3 (Cambridge, UK) and R (version 4.0.0) using the R2WinBUGS package.(17) For each model, three different chains with different initial values were run, each with at least 30,000 iterations, discarding the first 15,000 iterations and with the default thinning interval (equal to 3) set

by the R2WinBUGS package to compute summary estimates. We used trace plots to evaluate convergence for each chain for all component effects and all tested interactions between components. Minimally informative (non-Jeffrey's) prior distributions for the trials' baseline risks (defined as quit rates in control arms), component and interaction effects, and between-trial (heterogeneity) standard deviation (SD, measured on the log-odds scale) were chosen as in Freeman et al.(12) We assumed a common between-trial SD, and report results as ORs with 95% credibility intervals (CrIs). Models were compared using the Deviance Information Criteria (DIC); all models are presented regardless of DIC, to avoid overfitting, and as including models with very small improvement in DIC can result in excessively complex models. A reduction in DIC greater than 3 was the threshold used to indicate improved model fit.

We estimated odds ratios (ORs) and 95% credibility intervals (CrIs) for the effectiveness of the different components compared against each other, by component categories (Table 1). For example, for estimating the effect of an intervention provided individually versus as part of a group (on the logit scale), we subtracted the component effect of group delivery from that of individual delivery.

Next, we estimated ORs and 95% CrIs for interventions including pre-specified common combinations of components, with and without two-way interactions, compared with minimal intervention. With 36 components it is possible to include 630 two-way interactions. Removing clinically implausible interactions still leaves a large number of possible interactions. A CNMA model including all these interaction terms is unlikely to be estimable due to identifiability issues. Therefore, as a pragmatic approach, for the component combinations defined below, we compared the additive model with a model allowing for two-way interactions between the specified components. We tested the assumption of additive effects of components (on the logit scale) by adding all possible pre-defined two-way interactions between all components occurring in the same intervention. We limited interaction testing to those where the combination of components appeared in at least 20 arms. We had originally indicated we might also explore possible three- and four-way interactions, but did not proceed to this step as none of the few significant interactions observed involved the same components for a 3-way interaction to be suspected.

We further estimated the combined effect of combinations of components that are commonly delivered in conjunction with one another and that represent areas of clinical and research interest, using an interaction model focusing specifically on the (2-way) interactions between the components in the combinations of interest. The results of each model with interaction terms were compared with those of the additive model.

In our original analyses, we identified the components with apparently large beneficial effects, which could be combined in future interventions, but for which limited trial data currently exist (promising but under-evaluated combinations). In this paper, we estimate ORs and 95% CrIs for these combinations, with both additive and interaction models (the latter one focusing specifically on the (2-way) interactions between the components in the combinations of interest), focusing on interventions delivered remotely and/or with minimal in-person time to maximise potential reach and cost-effectiveness.

RESULTS

Three-hundred and twelve randomised controlled trials, representing 250,563 participants, 845 study arms, and 437 different combinations of components, were included (Figure S1). One hundred and twenty-five were judged to be at low risk of bias, 50 at high risk, and the remainder at unclear

risk. Most studies took place in the USA or Western Europe. The majority (195/312) took place in community settings. One hundred and forty studies recruited people explicitly on the basis of being motivated to quit smoking; eight explicitly recruited people not motivated to quit, and the remainder did not report selecting participants on the basis of motivation to quit. The median percentage of women was 54% (range 0% to 100%). Few studies reported on ethnicity. Full details of included studies have been published elsewhere.(3)

The component effects for the additive model are shown in Table 1. The component effects across all additive and interaction models are shown in Supplemental Table 1. DIC values for additive and interaction models ranged from 4135 to 4152 and suggested no improvement in model fit from adding interaction terms. Specific interactions are considered in relevant sections below. The following components were associated with higher odds of smoking cessation compared with minimal intervention, with 95% CrIs excluding no difference (Table 1): focus on how to quit, counselling, guaranteed financial incentives, and delivery of the intervention via text-message (SMS).. Provision of the intervention by a stop smoking advisor was associated with lower odds of smoking cessation.

1. Direct comparisons within component types

Overall, estimates regarding direct comparisons between components within nature and focus of the intervention groups were inconclusive (Figure 1). There was suggestive evidence that a focus on why to quit was less effective than a focus on how to quit (OR 0.85, 95% CrI 0.73 to 1.00). This was no longer apparent after removing studies at high risk of bias (Figure S2).

Provision of the intervention by a stop smoking advisor was associated with less benefit than delivery by a physician (OR 0.69, 95% CrI 0.52 to 0.93). Provision of the intervention by a stop smoking advisor was also associated with less benefit than delivery by a psychologist or counsellor (OR 0.76, 95% CrI 0.58 to 0.99) (Figure 1). The estimates were further from the null after excluding studies at high risk of bias, although with more uncertainty around them (Figure S2).

Delivery via SMS was associated with greater odds of smoking cessation than the following modes of delivery: face to face (SMS versus face-to-face, OR 1.39, 95% CrI 1.05 to 1.86), telephone (SMS versus telephone, OR 1.48, 95% CrI 1.13 to 1.94), print (SMS versus print, OR 1.44, 95% CrI 1.14 to 1.83) and (tentatively) web/computer (SMS versus web/computer, OR 1.34, 95% CrI 0.99 to 1.82) (Figure 2). Delivery of the intervention using a static video or providing access to a quit line were also associated with lower chances of smoking cessation than using SMS (video compared to SMS OR 0.58, 95% CrI 0.41 to 0.81; access to a quit line compared to SMS OR 0.57, 95% CrI 0.40 to 0.82). Delivery of the intervention using email was also associated with greater odds of smoking cessation than static video interventions (OR 1.93, 95% CrI 1.05 to 3.54) or quit line access (OR 1.94, 95% CrI 1.03 to 3.65). Delivery of the intervention individually was associated with lower odds of smoking cessation than as part of a group (OR 0.78, 95% CrI 0.64 to 0.95). Results for other direct comparisons between delivery modes were inconclusive.

In a sensitivity analysis removing studies at high risk of bias (Figure S3), the differences in the odds of smoking cessation between individual and group delivery and between SMS and face-to-face delivery were more uncertain though point estimates were similar. Whereas differences had not emerged in the original analysis including all studies, after removing studies at high risk of bias, telephone, print materials, or a static video were associated with less benefit than face-to-face delivery, with 95% CrIs excluding no difference. Audio recordings were associated with greater odds of smoking cessation than telephone, web/computer, print, or static video delivery, again with 95%

CrIs excluding no difference. There was insufficient data after removing studies at high risk of bias to calculate head-to-head comparisons between email and other delivery modes.

2. Investigating common combinations and potential interactions

Table 2 gives the ORs and 95% CrIs for 13 pre-defined combinations of components, calculated using both additive and interactive models. For five component combinations, interaction models were not estimated because there were fewer than 20 arms. In the other eight, there was no evidence that allowing for the interaction improved the fit of the model, and hence estimates presented below are based on additive models unless noted otherwise.

An intervention delivered with an SMS component was associated with greater odds of smoking cessation than minimal intervention, regardless of whether it also combined a face-to-face (OR 1.50, 95% CrI 1.13 to 2.01) or telephone component (OR 1.42, 95% CrI 1.09 to 1.85). None of the nature components were associated with greater odds of smoking cessation than minimal intervention (ORs between 1.05 and 1.08), but providing any pair of these components combined suggested (although with uncertainty, as 95% CrIs included no difference) increased odds of smoking cessation (with ORs between 1.13 and 1.16 in the additive model, and 1.41 to 1.49 in the interaction model). Tailoring did not increase the effect of an intervention delivered via the internet or app, but had an effect on interventions delivered using emails or SMS.

Commonly delivered component combinations were associated with increased abstinence compared with single components and additive models gave similar results to models allowing all two-way interactions (Table 3). These estimates were robust to the exclusion of studies at high risk of bias (Table S2). No interaction model improved fit over the additive model, and CIs overlapped between additive and interaction models.

3. Predicting the effects of combining promising but under-evaluated intervention components

In the additive model from our original CNMA analysis, we identified some components associated with increased odds of smoking cessation. We predicted the effect of interventions combining these components and obtained estimates of higher than two-fold increased odds of quitting compared with minimal intervention (Table 4). The predicted estimates of effect were similar between the additive model and interaction models. The estimates were similar after removing studies at high risk of bias (Table S3), except for an intervention including the email component which could not be estimated due to insufficient data.

DISCUSSION

Summary of main results

We found evidence that mode of delivery of behavioural support was associated with differences in effectiveness. Delivery via SMS was associated with greater effectiveness compared with delivery via telephone or via print, and groups associated with increased effectiveness compared with individual delivery. Commonly used combinations of mode of delivery (e.g. face-to-face counselling combined with telephone counselling, or tailored internet-based interventions combined with non-tailored SMS interventions) were associated with increased odds of quitting compared with minimal intervention. Components that were associated with effectiveness in the single component NMA were associated with greater effectiveness when combined. Where it was possible to test for interactions between components, we found no evidence for interaction effects with the additive and interaction models generally producing similar findings.

Strengths and limitations

It was possible within this analysis to examine a large number of combinations of components. We used input from key stakeholders consulted during the original Cochrane Review to concentrate on combinations that might best inform service delivery and future research. Despite the large number of trials and participants included, imprecision remains a key issue, with wide CrIs noted for many estimates. Moreover, interaction analyses could lack power to exclude moderate interaction effects and we cannot exclude them; it seems likely that simply adding in effective components ad infinitum would ultimately lead to diminishing returns in reality, implying interaction. However, one could argue that component effects and interactions associated with larger clinically relevant effects on smoking cessation should have been identified with our large sample. Finally, although the data are derived from randomised trials, CNMA is an observational analysis. Differences in effect between, for example, modes of delivery, could occur because of other differential aspects of the populations enrolled or characteristics of the interventions not modelled in our network.

The analyses were exploratory, not confirmatory. Effect estimates presented here need to be verified in randomised trials. For example, caution should be taken when interpreting results suggesting superiority of SMS to face-to-face delivery, given that some of the effect of 'face-to-face' may in effect be spread among the other components that accompany it (e.g. counselling, provider) in a way that SMS is less likely to be. In analyses of common combinations of components, the combined effect size of interventions including text messaging was not larger than other face-to-face interventions tested (Table 3). Model selection was partially dependent on our previous analysis and it may be that other combinations could be beneficial. There is no accepted way to categorise behavioural interventions for smoking cessation; our method was typical of the way that investigators in trials have categorised their interventions. Another approach could have been to categorise interventions using behaviour change techniques. Black and colleagues used this approach in a smaller review and found that techniques targeting associative (cues to prompt behaviour) and self-regulatory processes were associated with success in person-delivered interventions, and that interventions including rewards were associated with success in written interventions.(9) Mode of delivery was found to moderate intervention effects. Other categorisation systems may yield further insights. Component effectiveness may also be a function of temporal trends or setting; it is possible that different components work better in different populations. We had intended to explore this in our original Cochrane review but had little data with which to do so.

We limited inclusion of trials to those in existing Cochrane Reviews. Each contributing review had, however, undertaken rigorous searching. The main difficulty with this pragmatic approach is that behavioural interventions that are not yet subject to a Cochrane Review will not have been included, although we think that the library does include most common behavioural support modes and thereby most trials of behavioural support for smoking cessation with long-term cessation outcomes. In some areas, there were few studies contributing data to particular modes of delivery or content; here, future trials would greatly strengthen the evidence. We conducted the analyses in this paper to inform such studies, as the CNMA approach has enabled us to predict effect sizes in a way not afforded by traditional meta-analyses or network meta-analyses. We also could not detect interactions of combinations of components that had been infrequently tested. There is as yet no way to test for publication bias in CNMA; methods for this are needed, and we cannot rule it out.

Because of the need to ensure joint randomizability in CNMA, we excluded trials conducted exclusively in some subgroups of individuals who smoke, for example people living with mental illness. Future research is needed to examine whether component effectiveness is similar or different for these subgroups of individuals as well as by other potential moderators. This would

best be done using individual level data as opposed to study-level aggregates. The studies we included focus on cigarette smoking; further research also is needed to examine the effectiveness of components of behavioural interventions for quitting the use of other tobacco products. Our assumption that missing = smoking is standard in the field and across Cochrane reviews, but has been criticised (18); further work is needed to test whether this assumption meaningfully impacts effect estimates within meta-analyses.

Comparisons with other reviews

Pairwise comparisons of the type typically included in Cochrane Reviews provide effect estimates for intervention types, typically compared with no or minimal intervention. Our previous CNMA produced component estimates for, for example, individual counselling, that differ markedly from those in the Cochrane Review of individual counselling. This is because individual counselling in the CNMA 'strips out' effects of the nature of the counsellor, the content of the counselling, and its mode of delivery. Even combining components, as here, does not capture all of the content of an intervention and so estimates cannot be directly compared with those in Cochrane Reviews that are described in the same terms e.g. 'Individual Counselling for Smoking Cessation'. Of our direct comparisons, only that between individual and group can be compared with pairwise findings from traditional systematic reviews. Whereas we found evidence suggesting benefit of group over individual delivery modes, a pairwise meta-analysis found no difference (risk ratio (RR) 0.99, 95% confidence interval (CI) 0.76 to 1.28). However, CIs were wide in the latter and intervention content will have varied beyond just the mode of delivery.(19)

It is more reasonable to compare estimates from commonly used combinations we assessed to those from relevant pairwise meta-analyses as the combinations come close to 'adding back' all the relevant effects to form a package. Our models estimated that individual face-to-face counselling, delivered by a counsellor with a focus on how to quit and containing all three nature elements, might be associated with a 2.2 to 3.08 increased odds of quitting (additive and interaction estimates). Changing delivery mode to telephone counselling yielded point estimates of 2.08 and 2.57. Estimates from pairwise meta-analyses yielded slightly more conservative estimates but also clinically and statistically significant evidence of benefit, with risk ratios (RRs) of 1.57 (95% confidence interval (CI) 1.40 to 1.77; high-certainty) for individual face-to-face counselling compared with minimal intervention, and 1.38 (95% CI 1.19 to 1.61, moderate certainty) for telephone counselling.(10, 20) Our estimates for tailored internet interventions (providing why and how to quit content with motivation and self-regulation advice) ranged from 1.56 to 1.65; pairwise meta-analysis again found evidence of benefit but lower magnitude of effect (RR 1.15, 95% CI 1.01 to 1.30, low-certainty).(21) Point estimates for a non-tailored text message based intervention providing a why and how to quit focus, with motivation and self-regulation advice, ranged from 1.99 to 2.22; this compares with an RR of 1.54 (95% CI 1.19 to 2.00, moderate certainty) generated by pair-wise analysis.(22)

There are a number of reasons why our point estimates for interventions may be higher from the CNMA than in comparable pairwise meta-analyses from relevant Cochrane reviews. In the case of findings relating to counselling, not all of the studies in the individual reviews used all the components estimated in our CNMA, which may account for this. Additionally pairwise comparisons included active interventions (such as brief advice and/or self-help) as comparators, whereas effect estimates from our network meta-analysis are compared to no intervention only. As brief advice and self-help have proven effective at increasing quit rates, we would expect that our effect estimates, comparing to no stop smoking support or advice whatsoever, would be larger than those comparing to some sort of stop smoking support.(23, 24) Other research has indeed demonstrated that

comparator group content in trials of behavioural support for smoking cessation impacts effect estimates and can introduce variation in meta-analysis; CNMA is one way to overcome this issue.(25) Finally, ORs can be larger than RRs, making direct comparison of the two challenging. However, this is more of a risk for studies where events are common, which is not the case for smoking cessation trials, and hence renders this unlikely to be a major issue when it comes to comparability in this instance.(26) Ultimately, the individual studies in the pairwise analyses include a range of intervention components, not all of which will map to those tested in our model. Therefore, we are unable to conclude whether differences in estimates are due to genuine differences in effect based on intervention components, differences based on comparator group intensity, or due to differences in the statistical models.

Further research could explore the impact of these estimates on cost-effectiveness modelling. In our original review, we summarised evidence on comparative cost-effectiveness in the form of a Cochrane Brief Economic Commentary.(3) Comparisons were inconclusive with different cost-effectiveness analyses finding different results (e.g. some suggesting superiority of group to individual delivery, some suggesting the opposite). Decisions about intervention provision will in reality be based on both effectiveness and cost, and incorporating our estimates into cost-effectiveness modelling may yield further clarity for commissioners.

Conclusions

Behavioural counselling and guaranteed financial incentives are associated with the greatest degree of success; there was no evidence to suggest the contributing effect of these individual components was impacted by the other components they are delivered alongside. Incorporating additional components associated with effectiveness may further increase benefit. Further randomized controlled trials could investigate potential combinations of components in interventions delivered remotely, for which our model predicts optimum effectiveness; this includes guaranteed financial incentive programmes delivered via SMS, email, or mobile phone app, and behavioural counselling delivered via a mobile phone app, all with individual-level tailoring and a focus on why and how to quit.

Acknowledgements

This project was supported by the National Institute for Health Research (NIHR), via Cochrane Infrastructure and Cochrane Programme Grant funding to the Cochrane Tobacco Addiction Group, and via the NIHR Complex Reviews Support Unit (AS and SF). The views and opinions expressed herein are those of the authors and do not necessarily reflect those of the Systematic Reviews Programme, NIHR, National Health Service, or the Department of Health and Social Care. PA is funded by NIHR Oxford Biomedical Research Centre (BRC) and the NIHR Oxford and Thames Valley Applied Research Collaboration.

JMOM receive funding from the NIHR BRC, Oxford and the NIHR Applied Research Collaboration (ARC) Oxford and Thames Valley at Oxford Health NHS Foundation Trust.

TF receives funding from the NIHR Community Healthcare MedTech and In Vitro Diagnostics Co-operative at Oxford Health NHS Foundation Trust and the NIHR Applied Research Collaboration Oxford and Thames Valley at Oxford Health NHS Foundation Trust.

We thank Kerstin Frie, Moeko Hayashi, Thayla Santino, and Rodrigo Torres Castro for translating published reports of studies included in the network meta-analysis. We thank Sarah King and Karen Rees, freelance systematic reviewers, for their help with data extraction for the network meta-analysis.

Figures and tables, with legends

Table 1. Effect estimates of components evaluated in the CNMA for the re-analysis of the overview of behavioural therapies for smoking cessation compared to no intervention.

Component group[1] Component name	**N trials**	**N arms**	**N smokers**	**N quitters**	**OR (95% CrI)** [1,2]
Minimal intervention	58	58	22,998	1,151	1.00 (Reference)
Focus					
Why quit[2]	152	253	86,232	7,991	1.01 (0.89 to 1.16)
How to quit	226	425	141,707	14,964	**1.19 (1.01 to 1.41)**
Nature[3]					
Motivation	231	414	143,488	14,318	1.08 (0.96 to 1.22)
Self-regulation	257	483	158,222	16,780	1.05 (0.91 to 1.22)
Adjuvant activities	141	244	90,186	9,440	1.08 (0.95 to 1.23)
Behavioural					
Counselling	194	311	72,273	9,968	**1.44 (1.22 to 1.69)**
Biofeedback	27	38	8,511	975	1.10 (0.90 to 1.34)
Hypnotherapy	11	12	701	137	1.57 (0.91 to 2.74)
Exercise	17	21	3,154	389	0.99 (0.68 to 1.46)
Financial incentives: guaranteed	19	22	8,877	894	**1.46 (1.14 to 1.85)**
Financial incentives: not guaranteed	10	17	6,827	590	0.86 (0.56 to 1.32)
Tailoring	228	369	114,059	13,190	1.11 (0.98 to 1.26)
Intervention provider					
Nurse (general/specialist)	34	53	11,736	1,186	0.91 (0.72 to 1.17)
Stop smoking advisor	31	48	17,113	2,321	**0.77 (0.60 to 0.98)**
Psychologist/counsellor (as defined by study)	72	119	22,421	3,522	1.02 (0.85 to 1.22)
Physician	61	114	27,680	2,729	1.11 (0.88 to 1.40)
Pharmacist	4	7	936	82	1.16 (0.45 to 3.00)
Lay health advisor	8	9	2,881	352	1.34 (0.94 to 1.92)
Hypnotist	8	9	589	113	1.80 (0.88 to 3.74)

Exercise specialist	8	8	1,107	144	1.43 (0.82 to 2.49)
Other	22	36	8,386	827	1.04 (0.76 to 1.42)
Mode of delivery					
Group	75	130	15,574	3,127	1.16 (0.96 to 1.39)
Individual	185	322	88,569	10,077	0.90 (0.76 to 1.07)
Face-to-face	177	338	65,044	7,951	1.04 (0.86 to 1.26)
Telephone	94	139	47,029	6,076	0.98 (0.83 to 1.15)
Web/computer	50	84	41,002	4,166	1.08 (0.89 to 1.31)
Print	170	319	115,067	10,982	1.00 (0.88 to 1.15)
SMS	22	26	14,161	1,191	**1.45 (1.17 to 1.80)**
App	3	4	1,083	161	1.26 (0.62 to 2.56)
Video (static)	20	28	10,254	1,163	0.84 (0.65 to 1.07)
Video (interactive)	3	4	1,802	302	0.99 (0.43 to 2.26)
Audio	11	15	5,039	547	1.32 (0.91 to 1.92)
Interactive voice response	5	6	1,293	265	1.19 (0.79 to 1.81)
Quitline access	10	14	6,771	823	0.83 (0.62 to 1.12)
Email	4	7	1,847	202	1.61 (0.93 to 2.78)

[1]In the original model we included 38 components; in this re-analysis we did not include 'dentist' (provider) due to a paucity of studies, and combined general and specialist nurse because descriptions were often unclear. We did not include intensity components due to issues with reporting in original studies.

[2] This means focussing on the reasons for quitting smoking

[3] Motivation, self-regulation and adjuvant activities were defined as per Michie 2011

[4]The results shown correspond to the model assuming additive component effects.

[5] Estimates in bold denote statistical significance

[5].

Table 2. Effect estimates for additive and interaction models investigating possible added value of pre-specified components, compared to no intervention

					OR (95% CrI)	
Component / *Intervention*	**Trials**	**Arms**	**N**	**Quit**	**Additive model [1]**	**Interaction model [2]**
Face-to-face component	177	338	65,044	7,951	1.04 (0.86 to 1.26)	1.08 (0.80 to 1.47)
Telephone component	94	139	47,029	6,076	0.98 (0.83 to 1.15)	0.96 (0.69 to 1.34)
Face-to-face * Telephone interaction	51	71	14,571	2,042	n/a	0.91 (0.67 to 1.23)
Overall effect (compared to MI)					*1.02 (0.77 to 1.35)*	*0.94 (0.66 to 1.35)*
Face-to-face component	177	338	65,044	7,951	1.04 (0.86 to 1.26)	1.08 (0.80 to 1.47)
Print component	170	319	115,067	10,982	1.00 (0.88 to 1.15)	0.91 (0.73 to 1.14)
Face-to-face * Print interaction	91	144	32,762	3,660	n/a	1.07 (0.81 to 1.40)
Overall effect (compared to MI)					*1.04 (0.82 to 1.33)*	*1.05 (0.76 to 1.44)*
Telephone component	94	139	47,029	6,076	0.98 (0.83 to 1.15)	0.96 (0.69 to 1.34)
Print component	170	319	115,067	10,982	1.00 (0.88 to 1.15)	0.91 (0.73 to 1.14)
Telephone * Print interaction	57	81	32,770	3,818	n/a	1.18 (0.93 to 1.49)
Overall effect (compared to MI)					*0.99 (0.80 to 1.22)*	*1.03 (0.71 to 1.50)*
Face-to-face component	177	338	65,044	7,951	1.04 (0.86 to 1.26)	1.08 (0.80 to 1.47)
SMS component	22	26	14,161	1,191	1.45 (1.17 to 1.80)	1.39 (1.11 to 1.74)
Face-to-face * SMS interaction	7	9	1,978	327	n/a	n/a
Telephone component	94	139	47,029	6,076	0.98 (0.83 to 1.15)	0.96 (0.69 to 1.34)
SMS component	22	26	14,161	1,191	1.45 (1.17 to 1.80)	1.39 (1.11 to 1.74)
Telephone * SMS interaction	3	4	438	130	n/a	n/a
How to quit component	226	425	141,707	14,964	1.19 (1.01 to 1.41)	1.07 (0.67 to 1.70)
Why quit component	152	253	86,232	7,991	1.01 (0.89 to 1.16)	0.93 (0.58 to 1.49)
How to quit * Why quit interaction	70	92	37,824	3,590	n/a	1.07 (0.66 to 1.74)
Overall effect (compared to MI)					*1.21 (0.93 to 1.57)*	*1.07 (0.66 to 1.74)*
Motivation component	231	414	143,488	14,318	1.08 (0.96 to 1.22)	1.26 (0.84 to 1.91)
Self-regulation	257	483	158,222	16,780	1.05 (0.91 to 1.22)	1.19 (0.79 to 1.80)
Motivation * Self-regulation interaction	207	326	119,273	12,268	n/a	0.96 (0.65 to 1.40)
Overall effect (compared to MI)					*1.14 (0.94 to 1.37)*	*1.44 (0.92 to 2.24)*
Motivation component	231	414	143,488	14,318	1.08 (0.96 to 1.22)	1.26 (0.84 to 1.91)
Adjuvant activities	141	244	90,186	9,440	1.08 (0.95 to 1.23)	1.43 (1.00 to 2.04)
Motivation * Adjuvant activities interaction	106	161	61,395	6,334	n/a	0.83 (0.67 to 1.02)
Overall effect (compared to MI)					*1.16 (0.97 to 1.39)*	*1.49 (0.81 to 2.73)*
Self-regulation component	257	483	158,222	16,780	1.05 (0.91 to 1.22)	1.19 (0.79 to 1.80)
Adjuvant activities component	141	244	90,186	9,440	1.08 (0.95 to 1.23)	1.43 (1.00 to 2.04)
Self-regulation * Adjuvant activities interaction	133	214	79,390	8,628	n/a	0.83 (0.60 to 1.15)
Overall effect (compared to MI)					*1.13 (0.92 to 1.4)*	*1.41 (0.90 to 2.22)*
Tailoring component	228	369	114,059	13,190	1.11 (0.98 to 1.26)	1.10 (0.96 to 1.26)
Web/computer component	50	84	41,002	4,166	1.08 (0.89 to 1.31)	1.09 (0.81 to 1.46)
Tailoring * Web/computer interaction	40	56	25,159	2,897	n/a	0.96 (0.74 to 1.24)
Overall effect (compared to MI)					*1.20 (0.96 to 1.50)*	*1.14 (0.92 to 1.44)*
Tailoring component	228	369	114,059	13,190	1.11 (0.98 to 1.26)	1.10 (0.96 to 1.26)
App component	3	4	1,083	161	1.26 (0.62 to 2.56)	1.32 (0.64 to 2.73)
Tailoring * App interaction	2	2	658	109	n/a	n/a
Tailoring component	228	369	114,059	13,190	1.11 (0.98 to 1.26)	1.10 (0.96 to 1.26)
Email component	4	7	1,847	202	1.61 (0.93 to 2.78)	1.61 (0.93 to 2.80)
Tailoring * Email interaction	3	4	860	111	n/a	n/a

Tailoring component	228	369	114,059	13,190	1.11 (0.98 to 1.26)	1.10 (0.96 to 1.26)
SMS component	22	26	14,161	1,191	1.45 (1.17 to 1.80)	1.39 (1.11 to 1.74)
Tailoring * SMS interaction	15	18	8,289	992	n/a	n/a

[1] In the additive model, no interaction between components is assumed; therefore, the overall effect of an intervention including two components is equal to the sum of the log ORs for each component (or product of ORs for each component).

[2] One interaction model was ran for each intervention. In the interaction model, pairwise or two-way interactions between all the components in the intervention are assumed; therefore, the effect of an intervention including two components is equal to the sum of the log ORs for each component and their interaction (or product of ORs for each component and their interaction). For combination of components occurring in less than 20 arms, the interaction component was not estimated due to concerns about non-convergence, and therefore the overall effect is not reported.

Table 3. Effect estimates for additive and interaction models investigating effects of commonly delivered intervention components, compared to no intervention

Intervention	Model [1,2]	OR (95% CrI)
Tailored individual face-to-face counselling delivered by a counsellor with a focus on how to quit and all nature elements	Additive Interaction	2.20 (1.69 to 2.91) 3.08 (2.11 to 4.56)
Tailored individual telephone counselling delivered by a counsellor with a focus on how to quit and all nature elements	Additive Interaction	2.08 (1.67 to 2.62) 2.57 (1.95 to 3.42)
Tailored internet intervention providing why and how quit content with motivation and self-regulation advice	Additive Interaction	1.65 (1.26 to 2.15) 1.56 (1.09 to 2.24)
Non-tailored text message programme providing why and how quit content with motivation and self-regulation advice	Additive Interaction	1.99 (1.51 to 2.62) 2.22 (1.65 to 3.00)

[1] In the additive model, no interaction between components is assumed; therefore, the overall effect of an intervention including a number of components is equal to the sum of the log ORs for each component (or product of ORs for each component).

[2] One interaction model was ran for each intervention. In the interaction model, pairwise or two-way interactions between all the components in the intervention are assumed; therefore, the effect of an intervention including a number of components is equal to the sum of the log ORs for each component and all of their pairwise or two-way interactions (or product of ORs for each component and their two-way interactions). For combination of components occurring in less than 20 arms, the two-way interaction component was not estimated due to concerns about non-convergence. Interactions of higher order were not considered.

Table 4. Effect estimates for additive and interaction models for predicted promising interventions, compared to no intervention

Intervention	Model [1,2]	OR (95% CrI)
Guaranteed financial incentives intervention delivered via SMS, with tailoring and focus on why and how to quit	Additive	2.82 (1.89 to 4.24)
	Interaction	2.94 (1.91 to 4.52)
Guaranteed financial incentives intervention delivered via SMS, focus on why and how to quit (as above without tailoring)	Additive	2.54 (1.72 to 3.79)
	Interaction	2.68 (1.76 to 4.06)
Guaranteed financial incentives intervention delivered via email, with tailoring and focus on why and how to quit	Additive	2.83 (1.50 to 5.28)
	Interaction	3.26 (1.70 to 6.30)
Guaranteed financial incentives intervention delivered via mobile phone app, with tailoring, and focus on why and how to quit	Additive	2.21 (1.01 to 4.87)
	Interaction	2.62 (1.18 to 5.87)
Counselling delivered via mobile phone app, with tailoring and focus on how to quit	Additive	2.39 (1.14 to 5.03)
	Interaction	2.30 (1.09 to 4.82)
Guaranteed financial incentives and counselling intervention delivered via mobile phone app, with tailoring, and focus on why and how to quit	Additive	3.52 (1.59 to 7.87)
	Interaction	3.41 (1.49 to 7.87)

[1] In the additive model, no interaction between components is assumed; therefore, the overall effect of an intervention including a number of components is equal to the sum of the log ORs for each component (or product of ORs for each component).

[2] One interaction model was ran for each intervention. In the interaction model, pairwise or two-way interactions between all the components in the intervention are assumed; therefore, the effect of an intervention including a number of components is equal to the sum of the log ORs for each component and all of their pairwise or two-way interactions (or product of ORs for each component and their two-way interactions). For combination of components occurring in less than 20 arms, the two-way interaction component was not estimated due to concerns about non-convergence. Interactions of higher order were not considered.

Figure 1. Forest plot illustrating direct comparisons within motivational, behavioural, and provider component categories. Bold heading is reference group for each comparison.

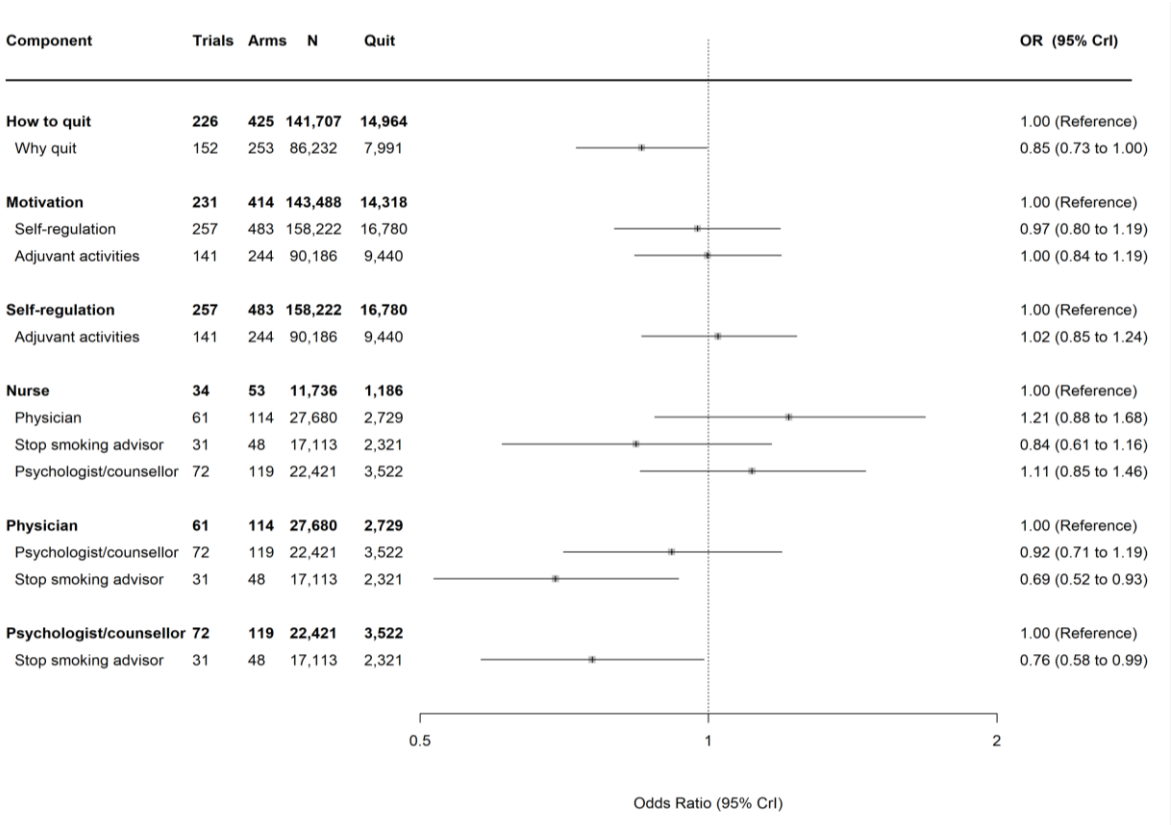
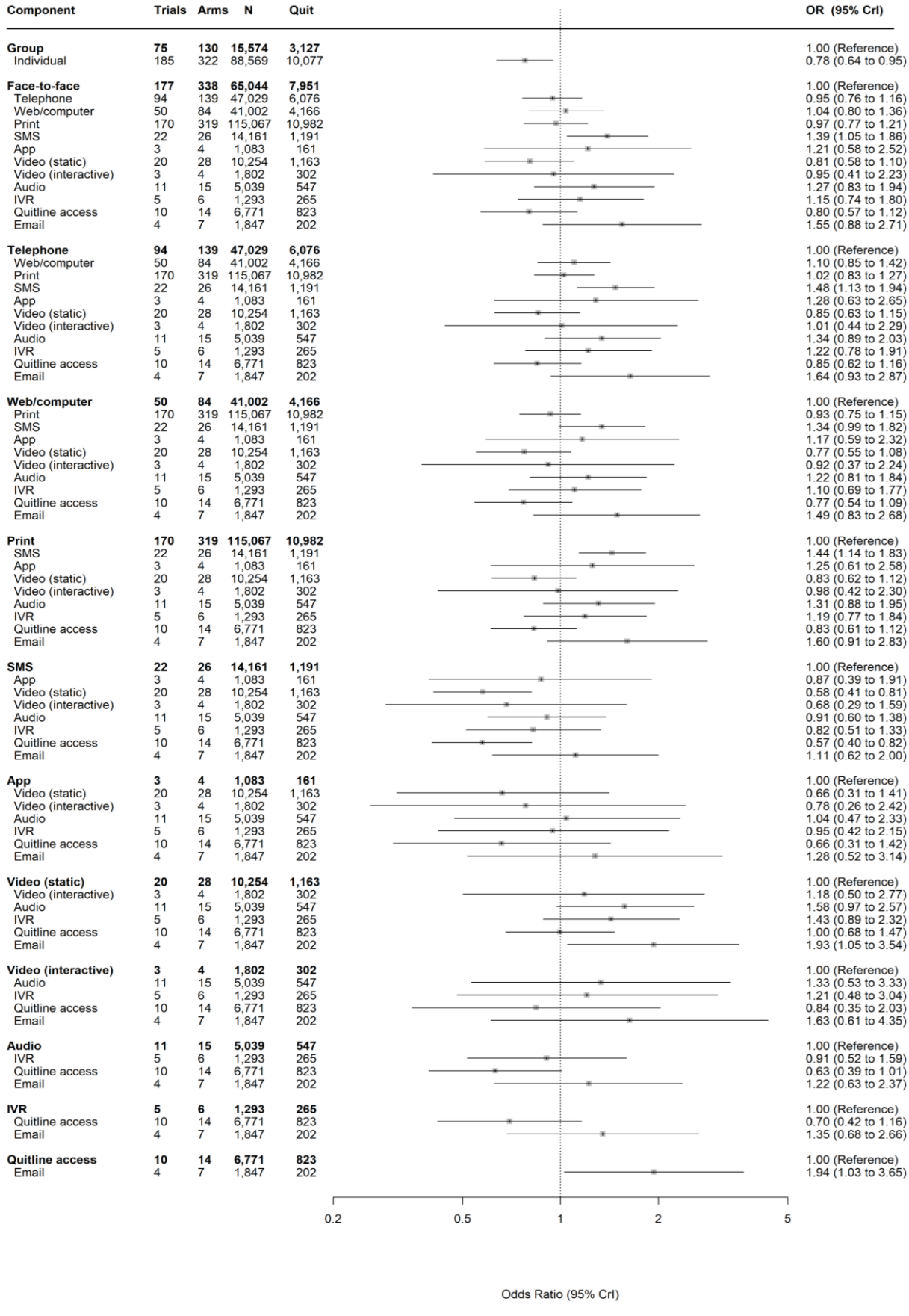


Figure 2. Forest plot illustrating direct comparisons within delivery mode component categories. Bold heading is reference group for each comparison.



REFERENCES

1. Organization WH. World Health Organization fact sheets. Tobacco 2018 [
2. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database of Systematic Reviews. 2013(5).
3. Hartmann-Boyce J, Livingstone-Banks J, Ordóñez-Mena JM, Fanshawe TR, Lindson N, Freeman SC, et al. Behavioural interventions for smoking cessation: an overview and network meta-analysis. Cochrane Database Syst Rev. 2021;1:Cd013229.
4. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ. 2004;328(7455):1519-.
5. Mons U, Müezzinler A, Gellert C, Schöttker B, Abnet CC, Bobak M, et al. Impact of smoking and smoking cessation on cardiovascular events and mortality among older adults: meta-analysis of individual participant data from prospective cohort studies of the CHANCES consortium. BMJ. 2015;350:h1551-h.
6. Müezzinler A, Mons U, Gellert C, Schöttker B, Jansen E, Kee F, et al. Smoking and all-cause mortality in older adults: results from the CHANCES consortium. American Journal of Preventive Medicine. 2015;49(5):e53-e63.
7. Ordóñez-Mena JM, Schöttker B, Mons U, Jenab M, Freisling H, Bueno-de-Mesquita B, et al. Quantification of the smoking-associated cancer risk with rate advancement periods: meta-analysis of individual participant data from cohorts of the CHANCES consortium. BMC Medicine. 2016;14(1):62-.
8. Hartmann-Boyce J, Hong B, Livingstone-Banks J, Wheat H, Fanshawe TR. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. Cochrane Database of Systematic Reviews. 2019(6).
9. Black N, Johnston M, Michie S, Hartmann-Boyce J, West R, Viechtbauer W, et al. Behaviour change techniques associated with smoking cessation in intervention and comparator groups of randomized controlled trials: a systematic review and meta-regression. Addiction2020. p. 2008-20.
10. Matkin W, Ordóñez-Mena JM, Hartmann-Boyce J. Telephone counselling for smoking cessation. Cochrane Database of Systematic Reviews. 2019(5).
11. Rouse B, Chaimani A, Li T. Network meta-analysis: an introduction for clinicians. Intern Emerg Med. 2017;12(1):103-11.
12. Freeman SC, Scott NW, Powell R, Johnston M, Sutton AJ, Cooper NJ. Component network meta-analysis identifies the most effective components of psychological preparation for adults undergoing surgery under general anesthesia. Journal of Clinical Epidemiology. 2018;98:105-16.
13. Hartmann-Boyce J, Livingstone-Banks J, Ordóñez-Mena JM, Fanshawe T, Lindson N, Freeman SC, et al. Behavioural programmes for smoking cessation: investigating interactions between behavioural, motivational, and delivery components using an existing component network meta-analysis. Open Science Framework. 2020:https://osf.io/v24kw/.
14. West R, Hajek P, Stead L, Stapleton J. Outcome criteria in smoking cessation trials: proposal for a common standard. Addiction (Abingdon, England). 2005;100(3):299-303.
15. Higgins JP, Green S, editor. Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from wwwhandbookcochraneorg.
16. Michie S, Hyder N, Walia A, West R. Development of a taxonomy of behaviour change techniques used in individual behavioural support for smoking cessation. Addict Behav. 2011;36(4):315-9.
17. Sturtz S, Ligges U, Gelman A. R2WinBUGS: a package for running WinBUGSfrom R. Journal of Statistical Software. 2005;12(3):1-16.

18. Hedeker D, Mermelstein RJ, Demirtas H. Analysis of binary outcomes with missing data: missing= smoking, last observation carried forward, and a little multiple imputation. Addiction. 2007;102(10):1564-73.
19. Stead LF, Carroll AJ, Lancaster T. Group behaviour therapy programmes for smoking cessation. Cochrane Database of Systematic Reviews. 2017(3).
20. Lancaster T, Stead LF. Individual behavioural counselling for smoking cessation. Cochrane Database of Systematic Reviews. 2017(3).
21. Taylor GM, Dalili MN, Semwal M, Civljak M, Sheikh A, Car J. Internet-based interventions for smoking cessation. Cochrane Database of Systematic Reviews. 2017(9).
22. Whittaker R, McRobbie H, Bullen C, Rodgers A, Gu Y, Dobson R. Mobile phone text messaging and app-based interventions for smoking cessation. Cochrane Database of Systematic Reviews. 2019(10).
23. Livingstone-Banks J, Ordóñez-Mena JM, Hartmann-Boyce J. Print-based self-help interventions for smoking cessation. Cochrane Database of Systematic Reviews. 2019(1).
24. Stead LF, Buitrago D, Preciado N, Sanchez G, Hartmann-Boyce J, Lancaster T. Physician advice for smoking cessation. Cochrane Database of Systematic Reviews. 2013(5).
25. Black N, Eisma MC, Viechtbauer W, Johnston M, West R, Hartmann-Boyce J, et al. Variability and effectiveness of comparator group interventions in smoking cessation trials: a systematic review and meta-analysis. Addiction (Abingdon, England). 2020;115(9):1607-17.
26. Cook TD. Advanced statistics: up with odds ratios! A case for odds ratios when outcomes are common. Academic Emergency Medicine. 2002;9(12):1430-4.