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# BMJ Open

**Impact of variation in intervention delivery and functions on the effectiveness of behavioural and mood management smoking cessation interventions for smokers with depression: A systematic review and meta-analysis protocol.**

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<b>Primary Subject Heading</b>:	Addiction
Secondary Subject Heading:	Mental health
Keywords:	Tobacco, Smoking cessation, Depression, Systematic review, Protocol, Intervention

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**TITLE**

Impact of variation in intervention delivery and functions on the effectiveness of behavioural and mood management smoking cessation interventions for smokers with depression: A systematic review and meta-analysis protocol.

**AUTHORS**

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1379

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Tobacco, Smoking cessation, Depression, Systematic review, Protocol, Intervention

## ABSTRACT

### Introduction

Tobacco is the world's leading preventable cause of disease and death. People with depression are twice as likely to smoke and are less responsive to standard tobacco treatments as compared to the general population. A Cochrane systematic review (Van der Meer 2013) of randomised controlled trials of smoking cessation treatment for smokers with current or historical depression found that adding psychosocial mood management to usual smoking treatment improved quit rates. However, the review did not examine if variation in intervention delivery or intervention functions impacted on treatment effectiveness.

With the aim of providing information to develop tailored approaches to treating smoking for people with depression we will add-on to the Cochrane review in three ways: 1) Use the Template for Intervention Description and Replication checklist (TIDieR) to determine if variations in delivery of mood management components impact on intervention effectiveness, 2) Use the Taxonomy of Behaviour Change techniques for smoking cessation to examine which behaviour change functions are most effective for smoking cessation in people with current depression, 3) Examine the difference in change in depression scores between intervention and control arms.

### Methods and Analysis

This review has been registered on PROSPERO (Review No. 70741). We will include randomised controlled trials of smokers with current depression as identified by the Cochrane review (Van der Meer 2013) and the in-progress update of the Cochrane review. We will use meta-regression to examine the impact of intervention components and behaviour change functions on treatment effectiveness, and a meta-analysis of the difference in change in depression scores between treatment arms from baseline to follow-up.

### Ethics and Dissemination

Ethical approval is not required for this study. We will disseminate the findings of this work at international and national conferences, and to the UK Centre for Tobacco and Alcohol Studies Smokers' Panel.

**STRENGTHS AND LIMITATIONS OF THIS STUDY**

- We will examine the impact of variation in intervention delivery and functions on treatment effectiveness using peer-reviewed checklists: The Behaviour Change Taxonomy (Michie et al, 2011), and Template for Intervention Description and Replication (TIDieR, Hoffmann et al, 2014).
- If analyses are possible, this study will provide causal effects of smoking treatment on depression symptoms in people with depression.
- May suffer from low power.
- May suffer from publication bias.

For peer review only

## BACKGROUND

Tobacco is the world's leading preventable cause of disease and death.<sup>1</sup> In the UK and in other developed nations smoking prevalence has declined substantially in the general population, but has remained largely unchanged in those with mental health problems resulting in an excess burden of smoking-related mortality in this group.<sup>2,3</sup> People with depression are twice as likely to smoke<sup>4,5</sup> and are less responsive to standard tobacco treatments than are the general population<sup>6,7</sup> leading to urgent calls for targeted smoking interventions.<sup>8</sup>

The Cochrane Group conducted a systematic review and meta-analysis of smoking cessation interventions for smokers with past or present depression. The review included pharmacological and behavioural interventions to aid cessation and found that adding psychosocial mood management to a usual smoking treatment (e.g., nicotine replacement therapy, telephone counselling, self-help website) moderately increased smoking cessation rates in people with current depression compared to usual smoking treatment alone, reporting a risk ratio of 1.47 (95% confidence interval: 1.13 to 1.92).<sup>9</sup> The review highlighted the importance of adding psychosocial techniques to handle depressive symptoms in standard smoking treatments for people with depression. However, in the meta-analysis there was variation between the included studies' direction of effect and it is possible that this variation may be in part related to differences in intervention delivery, intervention functions, or tailoring, for example. Further investigation into these potential modifiers will provide useful information for development of smoking cessation interventions for people with current depression.<sup>9</sup>

In addition, the review did not examine the impact of behavioural or psychological smoking cessation interventions on depression symptoms. This is an important question as many clinicians believe that smoking may offer mental health benefits, or that their patients' mental health may deteriorate upon cessation.<sup>10</sup> However, there are data from meta-analyses of cohort studies indicating that quitting smoking may improve depression,<sup>11</sup> but due to common pitfalls of observational cohort studies one cannot be sure that this is a causal association. If treating smoking is found to not worsen depression, then these data can be used to assure clinicians that they are not causing psychological harm by helping their patients to quit smoking.

In our review, we aim to add-on to the previous Cochrane review in three ways. We will:

- 1) Use the Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> to determine if variations in delivery of mood management components impact on intervention effectiveness.
- 2) Use the Taxonomy of Behaviour Change techniques for smoking cessation<sup>13</sup> to examine which behaviour change functions are most effective for smoking cessation in people with current depression.
- 3) Examine the difference in change in depression scores between intervention and control arms.

## METHODS

The study protocol will be registered in advance on the International Prospective Register of Systematic Reviews (PROSPERO; <http://www.crd.york.ac.uk/PROSPERO/>), uploaded to bioRxiv (<http://biorxiv.org/>), and submitted for publication to a peer-reviewed journal. All methods and study reporting will adhere to guidance described within the Cochrane Handbook for Systematic Reviews and Meta-analyses of Randomised Controlled Trials.<sup>14</sup>

### Inclusion criteria

- Study design: Randomised controlled trials only;
- Participants: Daily smokers with current depression, any definition of depression, no restrictions by physical or mental comorbidities;
- Intervention: Any smoking cessation intervention;
- Intervention delivery: Self-help, individual, group, internet;
- Control: Any (e.g., including self-help, no treatment, etc.);
- Outcome: Any ascertainment of smoking cessation;
- Follow-up: Follow up at a minimum of 6- months from the quit date.

### Outcomes:

- Smoking status at final follow-up;
- Change in depression scores from baseline to final follow-up.

### Search strategy

We will include relevant studies identified by a previously conducted Cochrane review of smoking cessation interventions for people with depression.<sup>9</sup> This review will be updated this year and we will also include relevant studies from the updated version of the review.

### Data extraction

We will extract the following data from included trials:

#### Trial methods:

Study design, setting, country, randomisation methods.

#### Participants:

Number of participants per intervention group, definition of depression, type of smoker, comorbid conditions, age, sex, ethnicity, level of education, nicotine dependence, mean/median number of cigarettes per day (CPD), depression type and severity.

#### Interventions:

Description of the interventions, the number of and function of behaviour change techniques used (where sufficient details are not reported in text, we will attempt to obtain intervention protocols), presence or absence of TIDieR checklist items.

Control:

Description of the control, the number of and function of behaviour change techniques used (where sufficient details are not reported in text, we will attempt to obtain intervention protocols), presence or absence of TIDieR checklist items.

Outcomes:

Smoking cessation status, biochemical validation, depression scores, length of follow-up.

### **Coding of Template for Intervention Description and Replication checklist (TIDieR)**

For study aim 1 we will use the Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> to determine if variations in delivery of mood management components impact on intervention effectiveness. We will use a modified version of the template as not all questions on the checklist are useful in the context of this study (e.g. "Describe any rationale, theory, or goal of the elements essential to the intervention"). Coding will be conducted separately by two researchers to confirm agreement.

### **Coding of behaviour change intervention functions:**

We will categorise behaviour change techniques according to their function and record whether the function was either absent or present during intervention delivery<sup>13</sup> (Table 2). Coding will be conducted separately by two researchers to confirm agreement.

### **Measures of treatment effect**

Smoking cessation (Study aims 1 & 2):

We will present treatment effects as risk ratios (RR) and 95% confidence intervals<sup>14</sup>. RRs will be calculated as follows: (number of participants who quit smoking in the intervention group/number of participants randomised to intervention group) divided by (number of participants who quit smoking in control group/number of participants randomised to the control group).

Difference in change in depression scores between trial arms (Study aim 3):

We will present the standardised mean difference (SMD), and 95% confidence intervals of change in depression scores between treatment arms, from baseline to follow-up.

### **Analysis**

All analyses will be conducted using Stata 14.

Study aim 1 - Do variations in delivery of mood management components impact on intervention effectiveness:

If there are sufficient data, we will conduct random effects meta-regression using the `metareg` command<sup>15</sup> in which modified TIDieR Checklist items (see Table 1) will be regressed on the study's effect estimate. First, univariate analyses will be conducted to determine the association between each item and the study effect size. Subsequently, items with the strongest association will be added to the meta-regression model first, and all other variables will be added in turn regardless of significance in the univariate model.



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3 Study aim 2 - Use the Taxonomy of Behaviour Change techniques for smoking cessation to examine  
4 which behaviour change functions are most effective for smoking cessation in people with current  
5 depression:  
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7 If there are sufficient data, we will conduct random effects meta-regression using the `metareg`  
8 command<sup>15</sup> in which behaviour change functions (see Table 2) will be regressed on the study's effect  
9 estimate. First, univariate analyses will be conducted to determine the association between each  
10 intervention component and the study effect size. Subsequently, variables with the strongest  
11 association will be added to the meta-regression model first, and all other variables will be added in  
12 turn regardless of significance in the univariate model.  
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15 Study aim 3 - Examine the difference in change in depression scores between intervention and  
16 control arms:  
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18 If there are sufficient data, we will use a generic inverse variance random effects model to pool the  
19 standardised mean difference (SMD) of change in depression scores in treatment and control arms,  
20 from baseline to follow-up. We will use a random effects model as it incorporates heterogeneity  
21 both within and between studies.  
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24 Statistical heterogeneity:

25 We will quantify statistical heterogeneity using  $I^2$  which describes the percentage (%) of between-  
26 study variability due to heterogeneity rather than chance; values over 50% suggest substantial  
27 heterogeneity, and values over 75% suggest considerable heterogeneity.<sup>14</sup>  $\tau^2$  will be used to test  
28 whether differences between studies' effect estimates are compatible with chance alone.<sup>16</sup>  
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31 Sensitivity and subgroup analyses:

32 We will conduct sensitivity analyses to examine if the following study characteristics influence the  
33 meta-analysis results: study quality (as measured by Cochrane's Risk of Bias tool), loss-to-follow-up,  
34 and severity of depression.  
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37 Assessment of publication bias:

38 We will examine funnel plots for evidence of asymmetry and conduct `egger` tests for evidence of  
39 small study bias using the `metabias` command.<sup>15</sup>  
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**ETHICAL APPROVAL**

Ethical approval is not required for this study.

**DISSEMINATION**

We will disseminate the findings of this work at international and national conferences, and to the UK Centre for Tobacco and Alcohol Studies Smokers' Panel.

**ACKNOWLEDGMENTS**

None.

**COMPETING INTERESTS**

All authors completed ICMJE Form for Disclosure of Potential Conflicts of Interest. GT, DT, RV, DK, BS report no competing interests. PA reports non-financial support from GSK, outside the submitted work. MM reports grants from Pfizer, outside the submitted work.

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**CONTRIBUTORSHIP STATEMENT**

All authors contributed to writing the manuscript and reviewed the final draft. GT, PA, RV, DK, BS, MM all contributed towards study design. DT is contributing to data extraction. GT and MM act as the guarantors of this review

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## TABLES

<b>Table 1. Modified version of Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> for use in meta-regression analysis*</b>	
<b>Item</b>	<b>Categories</b>
Materials for mood management (i.e., physical or informational materials used)	Paper-based information, website, homework, diary, audio information, etc.
Procedures for mood management: activities, procedures or activities used in the intervention to support activities	Relaxation techniques, mood monitoring, etc.
Did the participant see the same intervention provider for all mood management sessions?	Yes, no
Mood management provider	Nurse, psychologist, GP, counsellor, etc.
Training given to intervention provider?	Yes, no
Level of education of intervention provider	BSc, MSc, PhD
Mode of mood management intervention delivery	Individual, group
Location of mood management intervention	Hospital, participant's home, GP surgery, university, etc.
Number of mood management sessions	Continuous variable
Length of mood management session (minutes)	Continuous variable
Was the mood management intervention tailored to participant?	Yes, no
Number of mood management sessions tailored to participant?	Continuous variable
Was participant adherence to mood management intervention measured?	Yes, no
Did participants to adhere to mood management intervention.	Yes, no, or %
Was therapist adherence to mood management intervention measured? (Y/N)	Yes, no
Did therapists adhere to mood management programme? (Y/N)	Yes, no, or %
* The categories are likely to be further developed during data extraction to include new items.	

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<b>Behaviour change function</b>	<b>Examples of technique</b>
Specific focus on behaviour and addressing motivation	Provide information on consequences of smoking and smoking cessation
	Boost motivation and self-efficacy
	Provide feedback on current behaviour
Specific focus on behaviour and maximising self-regulatory capacity/skills	Advise on changing routine
	Advise on environmental restructuring
	Set graded tasks

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Page
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 5
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	n/a

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Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	n/a
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5-6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	6-7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	7
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6-7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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<b>Primary Subject Heading</b>:	Addiction
Secondary Subject Heading:	Mental health
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**AUTHORS**

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**WORD COUNT**

1379

**KEYWORDS**

Tobacco, Smoking cessation, Depression, Systematic review, Protocol, Intervention

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3 38 **ABSTRACT**

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5 39 **Introduction**

6 40 Tobacco is the world's leading preventable cause of disease and death. People with depression are  
7 41 twice as likely to smoke and are less responsive to standard tobacco treatments as compared to the  
8 42 general population. A Cochrane systematic review (Van der Meer 2013) of randomised controlled  
9 43 trials of smoking cessation treatment for smokers with current or historical depression found that  
10 44 adding psychosocial mood management to usual smoking treatment improved quit rates. However,  
11 45 the review did not examine if variation in intervention delivery or intervention functions impacted  
12 46 on treatment effectiveness.  
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16 48 With the aim of providing information to develop tailored approaches to treating smoking for people  
17 49 with depression we will add-on to the Cochrane review in three ways: 1) Use the Template for  
18 50 Intervention Description and Replication checklist (TIDieR) to determine if variations in delivery of  
19 51 mood management components impact on intervention effectiveness, 2) Use the Taxonomy of  
20 52 Behaviour Change techniques for smoking cessation to examine which behaviour change functions  
21 53 are most effective for smoking cessation in people with current depression, 3) Examine the  
22 54 difference in change in depression scores between intervention and control arms.  
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26 56 **Methods and Analysis**

27 57 This review has been registered on PROSPERO (ID: CRD42017070741). We will include randomised  
28 58 controlled trials of smokers with current depression as identified by the Cochrane review (Van der  
29 59 Meer 2013) and the in-progress update of the Cochrane review. We will use meta-regression to  
30 60 examine the impact of intervention components and behaviour change functions on treatment  
31 61 effectiveness, and a meta-analysis of the difference in change in depression scores between  
32 62 treatment arms from baseline to follow-up.  
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36 64 **Ethics and Dissemination**

37 65 Ethical approval is not required for this study. We will disseminate the findings of this work at  
38 66 international and national conferences, and to the UK Centre for Tobacco and Alcohol Studies  
39 67 Smokers' Panel.  
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3 68 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 4 69 • We will examine the impact of variation in intervention delivery and functions on treatment  
5 70 effectiveness using peer-reviewed checklists: The Behaviour Change Taxonomy (Michie et al,  
6 71 2011), and Template for Intervention Description and Replication (TIDieR, Hoffmann et al,  
7 72 2014).  
8 73 • If analyses are possible, this study will provide causal effects of smoking treatment on  
9 74 depression symptoms in people with depression.  
10 75 • May suffer from low power.  
11 76 • May suffer from publication bias.

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14 77 Not all intervention details may be reported. We will request intervention manuals from study  
15 78 authors, however these may not always be possible to obtain.  
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3 79 **BACKGROUND**  
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5 81 Tobacco is the world's leading preventable cause of disease and death.<sup>1</sup> In the UK and in other  
6 82 developed nations smoking prevalence has declined substantially in the general population, but has  
7 83 remained largely unchanged in those with mental health problems resulting in an excess burden of  
8 84 smoking-related mortality in this group.<sup>2,3</sup> People with depression are twice as likely to smoke<sup>4,5</sup> and  
9 85 are less responsive to standard tobacco treatments than are the general population<sup>6,7</sup> leading to  
10 86 urgent calls for targeted smoking interventions.<sup>8</sup>  
11 87

12 88 The Cochrane Group conducted a systematic review and meta-analysis of smoking cessation  
13 89 interventions for smokers with past or present depression. The review included pharmacological and  
14 90 behavioural interventions to aid cessation and found that adding psychosocial mood management to  
15 91 a usual smoking treatment (e.g., nicotine replacement therapy, telephone counselling, self-help  
16 92 website) moderately increased smoking cessation rates in people with current depression compared  
17 93 to usual smoking treatment alone, reporting a risk ratio of 1.47 (95% confidence interval: 1.13 to  
18 94 1.92).<sup>9</sup> The review highlighted the importance of adding psychosocial techniques to handle  
19 95 depressive symptoms in standard smoking treatments for people with depression. However, in the  
20 96 meta-analysis there was variation between the included studies' direction of effect and it is possible  
21 97 that this variation may be in part related to differences in intervention delivery, intervention  
22 98 functions, or tailoring, for example. Further investigation into these potential modifiers will provide  
23 99 useful information for development of smoking cessation interventions for people with current  
24 100 depression.<sup>9</sup>  
25 101

26 102 In addition, the review did not examine the impact of behavioural or psychological smoking  
27 103 cessation interventions on depression symptoms. This is an important question as many clinicians  
28 104 believe that smoking may offer mental health benefits, or that their patients' mental health may  
29 105 deteriorate upon cessation.<sup>10</sup> However, there are data from meta-analyses of cohort studies  
30 106 indicating that quitting smoking may improve depression,<sup>11</sup> but due to common pitfalls of  
31 107 observational cohort studies one cannot be sure that this is a causal association. If treating smoking  
32 108 is found to not worsen depression, then these data can be used to assure clinicians that they are not  
33 109 causing psychological harm by helping their patients to quit smoking.  
34 110

35 111 In our review, we aim to add-on to the 2013 Cochrane review<sup>9</sup> in three ways. We will:

- 36 112 1) Use the Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> to  
37 113 determine if variations in delivery of mood management components impact on  
38 114 intervention effectiveness.
  - 39 115 2) Use the Taxonomy of Behaviour Change techniques for smoking cessation<sup>13</sup> to examine  
40 116 which behaviour change functions are most effective for smoking cessation in people with  
41 117 current depression.
  - 42 118 3) Examine the difference in change in depression scores between intervention and control  
43 119 arms.
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3 120 **METHODS**

4 121 The study protocol has been registered in advance on the International Prospective Register of  
5 122 Systematic Reviews ((PROSPERO); ID: CRD42017070741; <http://www.crd.york.ac.uk/PROSPERO/>),  
6 123 and will be uploaded to bioRxiv (<http://biorxiv.org/>). All methods and study reporting will adhere to  
7 124 guidance described within the Cochrane Handbook for Systematic Reviews and Meta-analyses of  
8 125 Randomised Controlled Trials.<sup>14</sup>

9 126

10 127 **Search strategy**

11 128 We will include relevant studies identified by a previously conducted Cochrane review of smoking  
12 129 cessation interventions for people with depression, and from the Cochrane review update due to  
13 130 commence this year.<sup>9</sup> Studies have been identified from Cochrane Central Register of Controlled  
14 131 trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO using search terms related to 'depression', and  
15 132 'tobacco' or 'smoking' as recommended by the Tobacco Addiction Group and the Cochrane  
16 133 Depression, Anxiety and Neurosis Group. See the Tobacco Addiction Group Module in The Cochrane  
17 134 Library for full search strategies and the list of other resources searched.<sup>9</sup> This search strategy will be  
18 135 updated for additional relevant studies published from 2013. RV is the lead author for the Cochrane  
19 136 review published in 2013, and will lead on the Cochrane update of this review. To avoid duplicating  
20 137 efforts across teams and given the high reliance of Cochrane methods, RV will share the eligible  
21 138 studies prior to data extraction of the Cochrane update. We predict that this will take place in early  
22 139 2018.

23 140

24 141 **Inclusion criteria**

25 142 Inclusion criteria are based on those outlined in the 2013 Cochrane review.<sup>9</sup>

- 26 143
- 27 144 • Study design: Randomised controlled trials only;
  - 28 145 • Participants: Daily smokers with current depression, any definition of depression, no  
29 146 restrictions by physical or mental comorbidities;
  - 30 147 • Intervention: Any smoking cessation intervention;
  - 31 148 • Intervention delivery: Self-help, individual, group, internet;
  - 32 149 • Control: Any (e.g., including self-help, no treatment, etc.);
  - 33 150 • Outcome: Any ascertainment of smoking cessation;
  - 34 151 • Follow-up: Follow up at a minimum of 6- months from the quit date.

35 152

36 153 **Outcomes**

- 37 154
- 38 155 • Smoking status at final follow-up (same as the 2013 Cochrane review<sup>9</sup>)
  - 39 156 • Change in depression scores from baseline to final follow-up (not reported in the 2013  
40 157 Cochrane review<sup>9</sup>).
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**Data extraction**

We will use the following data as reported in the 2013 Cochrane review<sup>9</sup>:

- Trial methods - Study design, setting, country, randomisation methods.
- Participants - Number of participants per intervention group, definition of depression, type of smoker, comorbid conditions, age, sex, ethnicity, level of education, nicotine dependence, mean/median number of cigarettes per day (CPD), depression type and severity.
- Outcomes - Smoking cessation status, biochemical validation, depression scores, length of follow-up
- Measures of treatment effect, smoking cessation (Study aims 1 & 2): We will use the following outcome data as reported in the Cochrane review. The number of participants randomised to the intervention and control groups, and the number of participants who quit smoking in the intervention and control groups<sup>14</sup>

We will extract the following additional data not reported by in the 2013 Cochrane review<sup>9</sup>:

- Interventions - The number of and function of behaviour change techniques used (i.e. where sufficient details are not reported in text, we will attempt to obtain intervention protocols), presence or absence of TIDieR checklist items.
- Control - The number of and function of behaviour change techniques used (where sufficient details are not reported in text, we will attempt to obtain intervention protocols), presence or absence of TIDieR checklist items.
- Measures of treatment effect, depression symptoms (Study aim 3): For each trial arm, we will obtain mean depression scores and measure of variance at baseline and follow-up, mean differences and measures of variance from baseline to follow-up, or differences in change between trial arms' scores from baseline to follow-up and measures of variance.

**Coding of Template for Intervention Description and Replication checklist (TIDieR)**

The 2013 Cochrane review<sup>9</sup> did not extract any information relevant to the TIDieR checklist, these data are new to this review.

For study aim 1 we will use the Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> to determine if variations in delivery of mood management components impact on intervention effectiveness. We will use a modified version of the template as not all questions on the checklist are useful in the context of this study (Table 1) (e.g. "Describe any rationale, theory, or goal of the elements essential to the intervention"). Coding will be conducted separately by two researchers to confirm agreement.

**Coding of behaviour change intervention functions using the Behaviour Change Taxonomy (BCT)**

The 2013 Cochrane review<sup>9</sup> did not extract any information relevant to the BCT, these data are new to this review.

We will categorise behaviour change techniques according to their function and record whether the function was either absent or present during intervention delivery<sup>13</sup> (Table 2). Coding will be conducted separately by two researchers to confirm agreement.

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3 198 **Measures of treatment effect**

- 4 199 • Smoking cessation (Study aims 1 & 2): We will present treatment effects as risk ratios (RR)  
5 200 and 95% confidence intervals<sup>14</sup>. RRs will be calculated as follows: (number of participants  
6 201 who quit smoking in the intervention group/number of participants randomised to  
7 202 intervention group) divided by (number of participants who quit smoking in control  
8 203 group/number of participants randomised to the control group).
- 9 204 • Difference in change in depression scores between trial arms (Study aim 3): We will present  
10 205 the standardised mean difference (SMD), and 95% confidence intervals of change in  
11 206 depression scores between treatment arms, from baseline to follow-up.

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14 207 **Analysis**

15 208 We will conduct analyses using Stata 14 or Revman software.

16  
17 209 The following analytical procedures for each study aim are as follows:

- 18  
19 210 1. Do variations in delivery of mood management components impact on intervention  
20 211 effectiveness: If there are sufficient data, we will conduct random effects meta-regression using  
21 212 the `metareg` command<sup>15</sup> in which modified TIDieR Checklist items (see Table 1) will be  
22 213 regressed on the study's effect estimate. First, univariate analyses will be conducted to  
23 214 determine the association between each item and the study effect size. Subsequently, items  
24 215 with the strongest association will be added to the meta-regression model first, and all other  
25 216 variables will be added in turn regardless of significance in the univariate model.
- 26  
27 217 2. Use the Taxonomy of Behaviour Change techniques for smoking cessation to examine which  
28 218 behaviour change functions are most effective for smoking cessation in people with current  
29 219 depression: If there are sufficient data, we will conduct random effects meta-regression using  
30 220 the `metareg` command<sup>15</sup> in which behaviour change functions (see Table 2) will be regressed  
31 221 on the study's effect estimate. First, univariate analyses will be conducted to determine the  
32 222 association between each intervention component and the study effect size. Subsequently,  
33 223 variables with the strongest association will be added to the meta-regression model first, and all  
34 224 other variables will be added in turn regardless of significance in the univariate model.
- 35  
36 225 3. Examine the difference in change in depression scores between intervention and control  
37 226 arms: If there are sufficient data, we will use a generic inverse variance random effects model to  
38 227 pool the standardised mean difference (SMD) of change in depression scores in treatment and  
39 228 control arms, from baseline to follow-up. We will use a random effects model as it incorporates  
40 229 heterogeneity both within and between studies.

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43 230 Statistical heterogeneity: We will quantify statistical heterogeneity using  $I^2$  which describes the  
44 231 percentage (%) of between-study variability due to heterogeneity rather than chance; values over  
45 232 50% suggest substantial heterogeneity, and values over 75% suggest considerable heterogeneity.<sup>14</sup>  
46 233  $\tau^2$  will be used to test whether differences between studies' effect estimates are compatible with  
47 234 chance alone.<sup>16</sup>

48  
49 235 Sensitivity and subgroup analyses: We will conduct sensitivity analyses to examine if the following  
50 236 study characteristics influence the meta-analysis results: study quality (as measured by Cochrane's  
51 237 Risk of Bias tool), loss-to-follow-up, and severity of depression.

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53 238 Assessment of publication bias: We will examine funnel plots for evidence of asymmetry and  
54 239 conduct egger tests for evidence of small study bias using the `metabias` command.<sup>15</sup>

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3 240 **Dissemination**

4 241 We will disseminate the findings of this work at international and national conferences, and to the

5 242 UK Centre for Tobacco and Alcohol Studies Smokers' Panel.  
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For peer review only



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3 243 **DISCUSSION**

4 244 We will use the methods described in this protocol to determine: 1) if variations in delivery of mood  
5 245 management impact on smoking cessation intervention effectiveness in people with depression, 2)  
6 246 to examine which behaviour change functions are most effective for smoking cessation in people  
7 247 with depression, and 3) examine the difference in change in depression scores between intervention  
8 248 and control arms.

9 249  
10 250 We hold no strong hypotheses about which variations in mood management delivery/behaviour  
11 251 change functions will impact on treatment effectiveness. Potentially, intervention functions that  
12 252 focus on improving motivation to quit may strengthen the association between intervention and  
13 253 smoking cessation, as poor motivation is a hallmark symptom of depression. We do predict that at  
14 254 minimum smoking cessation Intervention will not be associated with a worsening in depression, and  
15 255 that intervention may be associated with an improvement in depression scores when compared to  
16 256 control.<sup>11</sup>

17 257

18 258 **Clinical applications**

19 259 If we are able to show that certain variations in delivery of mood management or behavioural  
20 260 support for smoking cessation are associated with higher abstinence rates, these data can be used  
21 261 by clinicians and researchers to optimise smoking cessation programmes for people with depression.  
22 262 Second, data pertaining to the impact of helping smokers with depression to quit smoking on  
23 263 depression symptoms will be imperative to smokers and clinicians.

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3 264 **ETHICAL APPROVAL**

4 265 Ethical approval is not required for this study.

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7 267 **ACKNOWLEDGMENTS**

8 268 None.

9 269

10 270 **COMPETING INTERESTS**

11 271 All authors completed ICMJE Form for Disclosure of Potential Conflicts of Interest. GT, DT, RV, DK, BS  
12 272 report no competing interests. PA reports non-financial support from GSK, outside the submitted  
13 273 work. MM reports grants from Pfizer, outside the submitted work.

14 274

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16  
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24 283 Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council,  
25 284 and the National Institute for Health Research, under the auspices of the UK Clinical Research  
26 285 Collaboration, is gratefully acknowledged. The funders have had no role in developing the protocol  
27 286 or study design.

28 287

29 288 **CONTRIBUTORSHIP STATEMENT**

30 289 All authors contributed to writing the manuscript and reviewed the final draft. GT, PA, RV, DK, BS,  
31 290 MM all contributed towards study design. DT contributed towards writing the manuscript. GT and  
32 291 MM act as the guarantors of this review.

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338 TABLES

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<b>Table 1. Modified version of Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> for use in meta-regression analysis*</b>	
<b>Item</b>	<b>Categories</b>
Materials for mood management (i.e., physical or informational materials used)	Paper-based information, website, homework, diary, audio information, etc.
Procedures for mood management: activities, procedures or activities used in the intervention to support activities	Relaxation techniques, mood monitoring, etc.
Did the participant see the same intervention provider for all mood management sessions?	Yes, no
Mood management provider	Nurse, psychologist, GP, counsellor, etc.
Training given to intervention provider?	Yes, no
Level of education of intervention provider	BSc, MSc, PhD
Mode of mood management intervention delivery	Individual, group
Location of mood management intervention	Hospital, participant's home, GP surgery, university, etc.
Number of mood management sessions	Continuous variable
Length of mood management session (minutes)	Continuous variable
Was the mood management intervention tailored to participant?	Yes, no
Number of mood management sessions tailored to participant?	Continuous variable
Was participant adherence to mood management intervention measured?	Yes, no
Did participants to adhere to mood management intervention.	Yes, no, or %
Was therapist adherence to mood management intervention measured? (Y/N)	Yes, no
Did therapists adhere to mood management programme? (Y/N)	Yes, no, or %
* The categories are likely to be further developed during data extraction to include new items.	

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<b>Behaviour change function</b>	<b>Examples of technique</b>
Specific focus on behaviour and addressing motivation	Provide information on consequences of smoking and smoking cessation
	Boost motivation and self-efficacy
	Provide feedback on current behaviour
Specific focus on behaviour and maximising self-regulatory capacity/skills	Advise on changing routine
	Advise on environmental restructuring
	Set graded tasks

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Page
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 5
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	n/a

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Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	n/a
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5-6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	6-7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	7
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6-7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

*From: Shamseer L, Moher D, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart L, PRISMA-P Group. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015: elaboration and explanation. BMJ. 2015 Jan 2;349(jan02 1):g7647.*

# BMJ Open

## Impact of variation in intervention delivery and intervention functions on the effectiveness of behavioural and mood management interventions for smoking cessation in people with depression: A systematic review and meta-analysis protocol.

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Note: The following files were submitted by the author for peer review, but cannot be converted to PDF. You must view these files (e.g. movies) online.	
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60**TITLE**

Impact of variation in intervention delivery and intervention functions on the effectiveness of behavioural and mood management interventions for smoking cessation in people with depression: A systematic review and meta-analysis protocol.

**AUTHORS**

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**WORD COUNT**

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**KEYWORDS**

Tobacco, Smoking cessation, Depression, Systematic review, Protocol, Intervention

**38 ABSTRACT****39 Introduction**

40 Tobacco is the world's leading preventable cause of disease and death. People with depression are  
41 twice as likely to smoke and are less responsive to standard tobacco treatments as compared to the  
42 general population. A Cochrane systematic review of randomised controlled trials of smoking  
43 cessation treatment for smokers with current or historical depression found that adding mood  
44 management to usual smoking treatment improved quit rates. However, the review did not examine  
45 if variation in intervention delivery or intervention functions impacted on treatment effectiveness.

46  
47 With the aim of providing information to develop tailored approaches to treating smoking for people  
48 with current depression we will add-on to the Cochrane review in three ways: 1) Use the Template  
49 for Intervention Description and Replication checklist to determine if variations in mood  
50 management delivery impact on intervention effectiveness, 2) Use the Taxonomy of Behaviour  
51 Change Techniques for smoking cessation to examine which behaviour change functions are most  
52 effective for smoking cessation in people with current depression, 3) Examine the difference in  
53 change in depression scores between intervention and control arms.

**54  
55 Methods and Analysis**

56 We will include randomised controlled trials of smokers with current depression as identified by the  
57 previous Cochrane review and the in-progress update of the Cochrane review. We will use meta-  
58 regression to examine 1) if variations in delivery of mood management impact on smoking cessation  
59 intervention effectiveness, 2) determine which behaviour change functions are most effective for  
60 smoking cessation and 3) use meta-analysis of the difference in change in depression scores  
61 between treatment arms from baseline to follow-up to determine if offering smoking cessation  
62 treatment causes psychological harm.

**63  
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65 Ethics and Dissemination**

66 Ethical approval is not required for this study. We will disseminate the findings of this work at  
67 conferences, and to relevant patient panels.

**68 Registration details**

69 PROSPERO ID: CRD42017070741

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3 70 **STRENGTHS AND LIMITATIONS OF THIS STUDY**

- 4 71 • We will examine the impact of variation in intervention delivery and intervention functions  
5 72 on treatment effectiveness using peer-reviewed checklists: The Behaviour Change  
6 73 Taxonomy, and Template for Intervention Description and Replication.  
7 74 • The study design may suffer from low power and/or publication bias.  
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3 75 **BACKGROUND**  
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5 77 Tobacco is the world's leading preventable cause of disease and death.<sup>1</sup> In the UK and in other  
6 78 developed nations smoking prevalence has declined substantially in the general population, but has  
7 79 remained largely unchanged in those with mental health problems resulting in an excess burden of  
8 80 smoking-related mortality in this group.<sup>2,3</sup> People with depression are twice as likely to smoke<sup>4,5</sup> and  
9 81 are less responsive to standard tobacco treatments than are the general population<sup>6,7</sup> leading to  
10 82 urgent calls for targeted smoking interventions.<sup>8</sup>  
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14 84 The Cochrane Group conducted a systematic review and meta-analysis of smoking cessation  
15 85 interventions for smokers with past or present depression. The review included pharmacological and  
16 86 behavioural interventions to aid cessation and found that adding mood management to a usual  
17 87 smoking treatment (e.g., nicotine replacement therapy, telephone counselling, self-help website)  
18 88 moderately increased smoking cessation rates in people with current depression compared to usual  
19 89 smoking treatment alone, reporting a risk ratio of 1.47 (95% confidence interval: 1.13 to 1.92).<sup>9</sup> The  
20 90 review highlighted the importance of adding psychological techniques to handle depressive  
21 91 symptoms in standard smoking treatments for people with depression. However, in the meta-  
22 92 analysis there was variation between the included studies' direction of effect and it is possible that  
23 93 this variation may be in part related to differences in intervention delivery or intervention functions,  
24 94 for example. Further investigation into these potential modifiers will provide useful information for  
25 95 development of smoking cessation interventions for people with current depression.<sup>9</sup>  
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30 97 In addition, the review did not examine the impact of behavioural or psychological smoking  
31 98 cessation interventions on depression symptoms. This is an important question as many clinicians  
32 99 believe that smoking may offer mental health benefits, or that their patients' mental health may  
33 100 deteriorate upon cessation.<sup>10</sup> However, there are data from meta-analyses of cohort studies  
34 101 indicating that quitting smoking may improve depression,<sup>11</sup> but due to common pitfalls of  
35 102 observational data one cannot be sure that this is a causal association. If treating smoking is found to  
36 103 not worsen depression, then these data can be used to assure clinicians that they are not causing  
37 104 psychological harm by helping their patients to quit smoking.  
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41 106 In our review, we aim to add-on to the 2013 Cochrane review<sup>9</sup> in three ways. We will:

- 42  
43 107 1) Use the Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> to  
44 108 determine if variations in mood management delivery impact on intervention effectiveness  
45 109 in people with depression.  
46 110 2) Use the Taxonomy of Behaviour Change techniques for smoking cessation<sup>13</sup> to examine  
47 111 which behaviour change functions are most effective for smoking cessation in people with  
48 112 current depression.  
49 113 3) Examine the difference in change in depression scores between intervention and control  
50 114 arms in people with current depression.  
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**METHODS**

The study protocol has been registered in advance on the International Prospective Register of Systematic Reviews ((PROSPERO); ID: CRD42017070741; <http://www.crd.york.ac.uk/PROSPERO/>). All methods and study reporting will adhere to guidance described within the Cochrane Handbook for Systematic Reviews and Meta-analyses of Randomised Controlled Trials.<sup>14</sup>

**Search strategy**

We will include relevant studies identified by a previously conducted Cochrane review of smoking cessation interventions for people with depression, and from the Cochrane review update due to commence this year.<sup>9</sup> Studies have been identified from the Cochrane Central Register of Controlled trials (CENTRAL), MEDLINE, EMBASE, and PsycINFO using search terms related to 'depression', and 'tobacco' or 'smoking' as recommended by the Tobacco Addiction Group and the Cochrane Depression, Anxiety and Neurosis Group. See the Tobacco Addiction Group Module in The Cochrane Library for full search strategies and the list of other resources searched.<sup>9</sup> This search strategy will be updated for additional relevant studies published from 2013. RV is the lead author for the Cochrane review published in 2013, and will lead on the Cochrane update of this review. To avoid duplicating efforts across teams and given the high reliance of Cochrane methods, RV will share the eligible studies prior to data extraction of the Cochrane update. We predict that this will take place in early 2018.

**Inclusion criteria**

Inclusion criteria are based on those outlined in the 2013 Cochrane review.<sup>9</sup>

- Study design: Randomised controlled trials only;
- Participants: Daily smokers with current depression, any definition of depression, no restrictions by physical or mental comorbidities;
- Intervention: Any smoking cessation intervention;
- Intervention delivery: Self-help, individual, group, internet;
- Control: Any (e.g., including self-help, no treatment, etc.);
- Outcome: Any ascertainment of smoking cessation;
- Follow-up: Follow up at a minimum of 6- months from the quit date.

**Outcomes**

- Smoking status at final follow-up (same as the 2013 Cochrane review<sup>9</sup>)
- Change in depression scores from baseline to final follow-up (not reported in the 2013 Cochrane review<sup>9</sup>).

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3 150 **Data extraction**

4 151 We will use the following data as reported in the 2013 Cochrane review<sup>9</sup>:

- 5  
6 152
- 7 153 • Trial methods - Study design, setting, country, randomisation methods.
  - 8 154 • Participants - Number of participants per intervention group, definition of depression, type  
9 155 of smoker, comorbid conditions, age, sex, ethnicity, level of education, nicotine dependence,  
10 156 mean/median number of cigarettes per day (CPD), depression type and severity.
  - 11 157 • Outcomes - Smoking cessation status, biochemical validation, depression scores, length of  
12 158 follow-up.
  - 13 159 • Measures of treatment effect, smoking cessation (Study aims 1 & 2): We will use the  
14 160 following outcome data as reported in the Cochrane review. The number of participants  
15 161 randomised to the intervention and control groups, and the number of participants who quit  
16 162 smoking in the intervention and control groups<sup>14</sup>

17  
18 162 We will extract the following additional data not reported by in the 2013 Cochrane review<sup>9</sup>:

- 19  
20 163
- 21 164 • Interventions - The number of and function of behaviour change techniques used (i.e. where  
22 165 sufficient details are not reported in text, we will attempt to obtain intervention protocols),  
23 166 and presence or absence of TIDieR checklist items.
  - 24 167 • Control - The number of and function of behaviour change techniques used (i.e. where  
25 168 sufficient details are not reported in text, we will attempt to obtain intervention protocols),  
26 169 and presence or absence of TIDieR checklist items.
  - 27 170 • Measures of treatment effect, depression symptoms (Study aim 3): For each trial arm, we  
28 171 will obtain mean depression scores and measure of variance at baseline and follow-up,  
29 172 mean differences and measures of variance from baseline to follow-up, or differences in  
30 173 change between trial arms' scores from baseline to follow-up and measures of variance.

31  
32 173 **Coding of Template for Intervention Description and Replication checklist (TIDieR)**

33 174 The 2013 Cochrane review<sup>9</sup> did not extract any information relevant to the TIDieR checklist<sup>12</sup>, these  
34 175 data are new to this review.

35  
36 176  
37 177 For study aim 1 we will use the TIDieR checklist<sup>12</sup> to determine if variations in mood management  
38 178 delivery impact on intervention effectiveness. We will use a modified version of TIDieR as not all  
39 179 items on the checklist are useful in the context of this study (Table 1) (e.g. "Describe any rationale,  
40 180 theory, or goal of the elements essential to the intervention"). Coding will be conducted separately  
41 181 by two researchers to confirm agreement.

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43 182  
44 183  
45 184 **Coding of behaviour change intervention functions using the Behaviour Change Taxonomy (BCT)**

46 185 The 2013 Cochrane review<sup>9</sup> did not extract any information relevant to the BCT<sup>13</sup>, these data are  
47 186 new to this review.

48  
49 187  
50 188 For study aim 2 we will code the number of behaviour change techniques, categorise the behaviour  
51 189 change techniques according to their function, and record whether the function was either absent or  
52 190 present during intervention delivery<sup>13</sup> (Table 2). Coding will be conducted separately by two  
53 191 researchers to confirm agreement.

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3 192 **Measures of treatment effect**

- 4 193 • Smoking cessation (Study aims 1 & 2): We will present treatment effects as risk ratios (RR)  
5 194 and 95% confidence intervals<sup>14</sup>. RRs will be calculated as follows: (number of participants  
6 195 who quit smoking in the intervention group/number of participants randomised to  
7 196 intervention group) divided by (number of participants who quit smoking in control  
8 197 group/number of participants randomised to the control group).
- 9 198 • Difference in change in depression scores between trial arms (Study aim 3): We will present  
10 199 the standardised mean difference (SMD), and 95% confidence intervals of change in  
11 200 depression scores between treatment arms, from baseline to follow-up.

12  
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14 201 **Analysis**

15 202 We will conduct analyses using Stata 14 or Revman software, and use the following analytical  
16 203 procedures to address each study aim:

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18 204 1. Do variations mood management delivery impact on intervention effectiveness: If there are  
19 205 sufficient data, we will conduct random effects meta-regression models using the `metareg`  
20 206 command<sup>15</sup> in which modified TIDieR checklist items (see Table 1) will be regressed on the  
21 207 study's effect estimate. First, univariate analyses will be conducted to determine the association  
22 208 between each item and the study effect size. Subsequently, items with the strongest association  
23 209 will be added to the meta-regression model first, and all other variables will be added in turn  
24 210 regardless of significance in the univariate model.

25  
26 211 2. Use the Taxonomy of Behaviour Change techniques for smoking cessation to examine which  
27 212 behaviour change functions are most effective for smoking cessation in people with current  
28 213 depression: If there are sufficient data, we will conduct random effects meta-regression models  
29 214 using the `metareg` command<sup>15</sup> in which behaviour change functions (see Table 2) will be  
30 215 regressed on the study's effect estimate. First, univariate analyses will be conducted to  
31 216 determine the association between each intervention function and the study effect size.  
32 217 Subsequently, variables with the strongest association will be added to the meta-regression  
33 218 model first, and all other variables will be added in turn regardless of significance in the  
34 219 univariate model.

35  
36 220 3. Examine the difference in change in depression scores between intervention and control  
37 221 arms: If there are sufficient data, we will use a generic inverse variance random effects model to  
38 222 pool the standardised mean difference (SMD) of change in depression scores in treatment and  
39 223 control arms, from baseline to follow-up. We will use a random effects model as it incorporates  
40 224 heterogeneity both within and between studies.

41  
42  
43 225 Statistical heterogeneity: We will quantify statistical heterogeneity using  $I^2$  which describes the  
44 226 percentage (%) of between-study variability due to heterogeneity rather than chance; values over  
45 227 50% suggest substantial heterogeneity, and values over 75% suggest considerable heterogeneity.<sup>14</sup>  
46 228 Tau<sup>2</sup> will be used to test whether differences between studies' effect estimates are compatible with  
47 229 chance alone.<sup>16</sup>

48  
49 230 Sensitivity and subgroup analyses: We will conduct sensitivity analyses to examine if the following  
50 231 study characteristics influence the meta-analysis results: study quality (as measured by Cochrane's  
51 232 Risk of Bias tool), loss-to-follow-up, and severity of depression.

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54 233 Assessment of publication bias: We will examine funnel plots for evidence of asymmetry and  
55 234 conduct egger tests for evidence of small study bias using the `metabias` command.<sup>15</sup>

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3 235 **Ethics and dissemination**

4 236 We will not require ethical approval for the conduct of this systematic review and meta-analysis. We  
5 237 will disseminate the findings of this work at international and national conferences, and to the UK  
6 238 Centre for Tobacco and Alcohol Studies Smokers' Panel.  
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3 239 **DISCUSSION**

4 240 We will use the methods described in this protocol to determine: 1) if variations in delivery of mood  
5 241 management impact on smoking cessation intervention effectiveness in people with depression, 2)  
6 242 to examine which behaviour change functions are most effective for smoking cessation in people  
7 243 with depression, and 3) examine the difference in change in depression scores between intervention  
8 244 and control arms.  
9 245

10 246 We hold no strong hypotheses about which variations in mood management delivery/behaviour  
11 247 change functions will impact on treatment effectiveness. Potentially, intervention functions that  
12 248 focus on improving motivation to quit may strengthen the association between intervention and  
13 249 smoking cessation, as poor motivation is a hallmark symptom of depression. We do predict that at  
14 250 minimum smoking cessation intervention will not be associated with a worsening in depression, and  
15 251 that intervention may be associated with an improvement in depression scores when compared to  
16 252 control.<sup>11</sup>  
17 253

18 254 **Clinical applications**

19 255 If we can show that certain variations in delivery of mood management or behavioural support for  
20 256 smoking cessation are associated with higher abstinence rates, these data can be used by clinicians  
21 257 and researchers to optimise smoking cessation programmes for people with depression. Second,  
22 258 data pertaining to the impact of helping smokers with depression to quit smoking on depression  
23 259 symptoms will be imperative to smokers and clinicians.  
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3 260 **ETHICAL APPROVAL**

4 261 Ethical approval is not required for this study.

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6  
7 263 **ACKNOWLEDGMENTS**

8 264 None.

9 265

10 266 **COMPETING INTERESTS**

11 267 All authors completed ICMJE Form for Disclosure of Potential Conflicts of Interest. GT, DT, RV, DK, BS  
12 268 report no competing interests. PA reports non-financial support from GSK, outside the submitted  
13 269 work. MM reports grants from Pfizer, outside the submitted work.

14 270

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25 281 Collaboration, is gratefully acknowledged. The funders have had no role in developing the protocol  
26 282 or study design.

27 283

28 284 **CONTRIBUTORSHIP STATEMENT**

29 285 All authors contributed to writing the manuscript and reviewed the final draft. GT, PA, RV, DK, BS,  
30 286 MM all contributed towards study design. DT contributed towards writing the manuscript. GT and  
31 287 MM act as the guarantors of this review.

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334 TABLES

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<b>Table 1. Modified version of Template for Intervention Description and Replication checklist (TIDieR)<sup>12</sup> for use in meta-regression analysis*</b>	
<b>Item</b>	<b>Categories</b>
Materials for mood management (i.e., physical or informational materials used)	Paper-based information, website, homework, diary, audio information, etc.
Procedures for mood management: activities, procedures or activities used in the intervention to support activities	Relaxation techniques, mood monitoring, etc.
Did the participant see the same intervention provider for all mood management sessions?	Yes, no
Mood management provider	Nurse, psychologist, GP, counsellor, etc.
Training given to intervention provider?	Yes, no
Level of education of intervention provider	BSc, MSc, PhD
Mode of mood management intervention delivery	Individual, group
Location of mood management intervention	Hospital, participant's home, GP surgery, university, etc.
Number of mood management sessions	Continuous variable
Length of mood management session (minutes)	Continuous variable
Was the mood management intervention tailored to participant?	Yes, no
Number of mood management sessions tailored to participant?	Continuous variable
Was participant adherence to mood management intervention measured?	Yes, no
Did participants to adhere to mood management intervention.	Yes, no, or %
Was therapist adherence to mood management intervention measured? (Y/N)	Yes, no
Did therapists adhere to mood management programme? (Y/N)	Yes, no, or %
* The categories are likely to be further developed during data extraction to include new items.	

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<b>Behaviour change function</b>	<b>Examples of technique</b>
Specific focus on behaviour and addressing motivation	Provide information on consequences of smoking and smoking cessation
	Boost motivation and self-efficacy
	Provide feedback on current behaviour
Specific focus on behaviour and maximising self-regulatory capacity/skills	Advise on changing routine
	Advise on environmental restructuring
	Set graded tasks

**PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol\***

Section and topic	Item No	Checklist item	Page
<b>ADMINISTRATIVE INFORMATION</b>			
Title:			
Identification	1a	Identify the report as a protocol of a systematic review	1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such	n/a
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number	2, 5
Authors:			
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author	1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review	8
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments	n/a
Support:			
Sources	5a	Indicate sources of financial or other support for the review	8
Sponsor	5b	Provide name for the review funder and/or sponsor	8
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol	8
<b>INTRODUCTION</b>			
Rationale	6	Describe the rationale for the review in the context of what is already known	4
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO)	4
<b>METHODS</b>			
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review	5-6
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage	5
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated	n/a

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Study records:			
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review	6
Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis)	n/a
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators	6
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications	6
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale	5-6
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis	7
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised	6-7
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as $I^2$ , Kendall's $\tau$ )	6-7
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression)	7
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned	6-7
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies)	6-7
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE)	n/a

**\* It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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