ADDICTION
SSA SOCIETY FOR THE STUDY OF ADDICTION
REVIEW
doi:10.1111/add.15614

Predictors of recruitment and retention in randomized controlled trials of behavioural smoking cessation interventions: a systematic review and meta-regression analysis

Alessio Bricca[1,2,3], Zoe Swithenbank[1,4], Neil Scott[5], Shaun Treweek[6], Marie Johnston[1], Nicola Black[1,7], Jamie Hartmann-Boyce[8], Robert West[9], Susan Michie[10] & Marijn de Bruin[1,11]

Health Psychology Group, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, UK,[1] Research Unit for Musculoskeletal Function and Physiotherapy, Department of Sports Science and Clinical Biomechanics, University of Southern Denmark, Odense, Denmark,[2] The Research Unit PROgrez, Department of Physiotherapy and Occupational Therapy, Næstved-Slagelse-Ringsted Hospitals, Slagelse, Denmark, Slagelse, Denmark,[3] Public Health Institute, Liverpool John Moores University, Liverpool, UK,[4] Medical Statistics Team, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, Scotland, UK,[5] Health Services Research Unit, University of Aberdeen, Aberdeen, Scotland, UK,[6] Technology Addiction Team, Brain and Mind Centre, University of Sydney, Sydney, Australia,[7] Nuffield Department of Primary Care Health Sciences and National Institute for Health Research Oxford Biomedical Research Centre, University of Oxford, Oxford, UK,[8] Health Behaviour Research Centre, Department of Epidemiology and Public Health, University College London, London, UK,[9] Centre for Behaviour Change, University College London, London, UK[10] and Radboud Institute for Health Sciences, IQ Healthcare, Radboud University Medical Centre, Nijmegen, the Netherlands[11]

ABSTRACT

Aim To investigate predictors of participant eligibility, recruitment and retention in behavioural randomized controlled trials (RCTs) for smoking cessation. **Method** Systematic review and pre-specified meta-regression analysis of behavioural RCTs for smoking cessation including adult (≥ 18-year-old) smokers. The pre-specified predictors were identified through a literature review and experts' consultation and included participant, trial and intervention characteristics and recruitment and retention strategies. Outcome measures included eligibility rates (proportion of people eligible for the trials), recruitment rates, retention rates and differential retention rates. **Results** A total of 172 RCTs with 89 639 participants. Eligibility [median 57.6%; interquartile range (IQR) = 34.7–83.7], recruitment (median 66.4%; IQR = 42.7–85.2) and retention rates (median 80.5%; IQR = 68.5–89.5) varied considerably across studies. For eligibility rates, the recruitment strategy appeared not to be associated with eligibility rates. For recruitment rates, use of indirect recruitment strategies (e.g. public announcements) [odds ratio (OR) = 0.30, 95% confidence interval (CI) = 0.11–0.82] and self-help interventions (OR = 0.14, 95% CI = 0.03–0.67) were associated with lower recruitment rates. For retention rates, higher retention was seen if the sample had ongoing physical health condition/s (OR = 1.66, 95% CI = 1.04–2.63), whereas lower retention was seen amongst primarily female samples (OR = 0.83, 95% CI = 0.71–0.98) and those motivated to quit smoking (OR = 0.74, 95% CI = 0.55–0.99) when indirect recruitment methods were used (OR = 0.60, 95% CI = 0.38–0.97) and at longer follow-up assessments (OR = 0.83, 95% CI = 0.79–0.87). For differential retention, higher retention in the intervention group occurred when the intervention but not comparator group received financial incentives for smoking cessation (OR = 1.35, 95% CI = 1.02–1.77). **Conclusions** In randomized controlled trials of behavioural smoking cessation interventions, recruitment and retention rates appear to be higher for smoking cessation interventions that include a person-to-person rather than at-a-distance contact; male participants, smokers with chronic conditions, smokers not initially motivated to quit and shorter follow-up assessments seems to be associated with improved retention; financial incentive interventions improve retention in groups receiving them relative to comparison groups.

Keywords Behaviour change techniques, differential attrition, randomised controlled trials, recruitment, retention, smoking cessation.

Correspondence to: Alessio Bricca, Research Unit for Musculoskeletal Function and Physiotherapy, Institute of Sports Science and Clinical Biomechanics, University of Southern Denmark, Campusvej 55, 5230 Odense M, Denmark. E-mail: abricca@health.sdu.dkSubmitted 14 December 2020; initial review completed 6 April 2021; final version accepted 9 June 2021

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INTRODUCTION

Recruiting people into and retaining people in randomized controlled trials (RCTs) is challenging [1], but essential for the internal and external validity of the study. For example, 25% of RCTs do not reach the planned sample size within target time-frames [2] and hence require funding extensions [3]. While there are several systematic reviews concerning recruitment and retention in RCTs from a wide range of medical fields [4], knowledge regarding which factors predict recruitment and retention in behavioural RCTs of smoking cessation intervention is limited [5].

In RCTs of behavioural smoking cessation interventions recruitment and retention rates vary considerably [5,6]. A systematic review of behavioural RCTs reports recruitment rates, i.e. the proportion of eligible individuals recruited, ranging from 4 to 95% and retention rates from 36 to 100% [7]. Additionally, retention rates may vary across intervention and comparator groups of the same study [8]. This may negatively affect both external and internal validity, constituting another source of uncertainty for the analysis and interpretation of the results. Less is known about which strategies are best at identifying eligible participants [9], although this is crucial in the recruitment process. Taken together, these considerations highlight the importance of identifying factors that may improve the recruitment and retention processes of RCTs.

In the smoking cessation field, results from individual studies suggest that participant characteristics (e.g. age) [10–12], recruitment and retention strategies (e.g. approaching participants individually) [13], trial characteristics (e.g. the use of financial incentives for participation) [14] and intervention characteristics (e.g. the mode or format of intervention delivery) [15,16] may influence recruitment and retention rates. However, factors associated with recruitment and retention in smoking cessation interventions have not been investigated systematically. To fill this gap, we aimed to ascertain predictors of recruitment and attrition rates across 172 behavioural RCTs of smoking cessation interventions included in the IC-SMOKE systematic review project [17]. The specific aims of this study are to investigate which factors are associated with: (1) eligibility rates (i.e. the proportion of people screened who are eligible), (2) recruitment rates (i.e. the proportion of eligible people randomized), (3) retention rates (i.e. the proportion of people randomized who provide the gold-standard outcome—biochemically verified smoking cessation outcomes [18] and (4) differential retention rates (i.e. the proportion retention in the intervention minus the comparator group). The results of this study may thus provide funders and researchers with the information they need to budget for and increase participation in smoking cessation research trials.

METHOD

The protocol and the statistical analysis plan for this work were published prior to commencing the project (PROSPERO CRD42019121453, and https://osf.io/5er49/). Inclusion criteria, search methods and data collection methods are based on the IC-SMOKE project [17]. The overall aim of the IC-SMOKE project is to assess the effectiveness of smoking cessation interventions and their active ingredients. The IC-SMOKE project is an ongoing systematic review including 172 behavioural smoking cessation randomized controlled trials, published between 1996 and 2018, including adult smokers and using behavioural interventions (with or without pharmacotherapy) compared to a different behaviour change intervention, treatment-as-usual, pharmacotherapy alone or no treatment. A pragmatic choice was made by the IC-SMOKE advisory board to include trials performed not earlier than 1996, as they are more likely to reflect current practice. The first search of the IC-SMOKE project was conducted in November 2015 and included 142 trials. For this systematic review and meta-regression analysis the database was updated (search: October 2018) and includes 172 trials.

In this project RCTs were identified from the Cochrane Tobacco Addiction Group Specialized Register (CTAGSR). As of 2018, this register was developed through continued and regular electronic searching of MEDLINE, EMBASE and PsycINFO, together with hand-searching of specialist journals, conference proceedings and reference lists of previous trials and overviews.

All studies in the CTAGSR register were screened for inclusion. Two reviewers independently screened titles and abstracts and all studies deemed eligible by at least one of the reviewers were checked independently in full text by the same two reviewers. Data were extracted independently two reviewers and for all the studies from all published information sources we could identify, i.e. trial paper, supplements, protocols and study websites. Throughout the study selection process and data extraction, a third reviewer was contacted to resolve the disagreement by discussion. Additionally, authors were contacted by e-mail (including two reminders) to send additional materials (such as leaflets and website materials) describing in detail the interventions delivered to both the intervention and comparator groups of the studies, clarifications of the recruitment and retention strategy used and the flow of the participants included. If no response was received, we e-mailed the second and last authors, followed by the middle authors.

Selection and classification for predictors

Based on a systematic search of the literature and input from experts we a priori-identified factors (i.e. predictors) that may influence the recruitment process (eligibility

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and recruitment rates) [4,9,19–22] and retention [10,11,14,16,22–29] in smoking cessation RCTs and grouped the identified predictors into four categories: participant characteristics (e.g. age and gender), recruitment strategies (e.g. recruitment via poster/flyers or in-person), retention strategies (e.g. use of financial incentives for participating in follow-up assessments), trial characteristics (e.g. length of study follow-up post-randomization) and intervention characteristics [e.g. number of behaviour change techniques (BCTs) for smoking cessation and treatment engagement]. BCTs are 'an observable, replicable and irreducible component of an intervention designed to alter or redirect causal processes that regulate behaviour; that is, a technique is proposed to be an 'active ingredient' (e.g. feedback, self-monitoring, reinforcement)' [30]. All potential predictors are measured at the study level in this study (e.g. average participant age) and definitions are given in Table 1 together with the pre-specified hypothesis for their association with recruitment and retention. Note that trial retention is distinct from intervention adherence: we are interested in measures to improve participants' provision of outcome data, not in increasing adherence to the intervention itself. The latter is important, but not the focus of our work. Details of their selection and classification is discussed in detail in the pre-published analysis plan (https://osf.io/5er49/).

Statistical analysis

We conducted multi-level meta-regression analyses, using exact binomial likelihoods [31], with a continuous-time autoregressive structure (CAR) to examine the association between potential predictors and:

1. Eligibility rates (number randomized + number declined to participate although being eligible)/number assessed for eligibility).
2. Recruitment rates (number randomized/number eligible).
3. Retention rates (number providing biochemically verified outcomes at any or follow-up assessment/number randomized).
4. Differential retention rates (difference in number providing biochemically verified outcomes in the intervention group and number providing biochemically verified outcomes in the comparator group/number randomized).

All statistical analyses were performed in RStudio version 3.6.0 using the Metafor package (https://wviechtb.github.io/metafor/reference/rma.mv.html) [32].

For the prediction of eligibility and recruitment we performed trial-level analyses and used the 'rma.uni' command to fit mixed-effects meta-regression models. For retention and differential retention rates we fitted a mixed-effects meta-regression model using the 'rm.mv' command, which allowed data from three levels (time-points within study arms within studies) to be incorporated. When incorporating multiple time-points per study, a continuous-time autoregressive structure was used for the variance–covariance matrix, as the number of available time-points varied.

The outcomes of interest were logit-transformed proportions, as outcomes were bounded by 0 and 1. For differential retention, we used the difference in retention rates between treatment and control group. We present the estimates as odds ratios (OR) with 95% confidence intervals (CI) and *P*-values. For all the models, we examined Cook's distances, HAT values and studentized residuals to check the model's assumptions. Missing values of nicotine dependency, assessed with the Fagerström Test for Nicotine Dependence, were imputed based on the number of cigarettes smoked per day when available. The dichotomous predictor had to have sufficient variability (i.e. at least 10% 0s or 1s) to be included in the models. An alpha level of 0.05 was used to define statistical significance.

Sensitivity analyses

We performed sensitivity analyses to investigate the impact of continent of origin of the study in the meta-regressions for eligibility, recruitment and retention rates. In the absence of existing evidence on this topic, these analyses were exploratory. Countries were grouped as follows: Europe (Denmark, France, Germany, Netherlands, Norway, Spain, Sweden, Switzerland, Turkey, United Kingdom), Oceania (Australia and New Zealand), North America (United States and Canada) and Asia (China, Hong Kong, Japan, South Korea, Malaysia and Pakistan). Additionally, we performed a sensitivity analysis for retention rates by restricting the analysis to studies that delivered the intervention interpersonally (i.e. individually or in-group). The rationale for this analysis was because interventions delivered interpersonally have been shown to promote higher smoking cessation rates [33].

Risk of bias

Risk of bias was assessed using the Cochrane Risk of Bias version 1. Risk of bias assessment was performed independently by two reviewers and disagreements were resolved by discussion with a third reviewer, following the recommendations from the Cochrane Handbook for Systematic Reviews of Interventions [34]. The risk of bias was assessed regarding the risk of selection bias, detection bias, attrition bias, reporting bias and other bias. Each of the following listed domains was assessed as adequate, unclear or inadequate: sequence generation, allocation concealment,

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Table 1 Predictors included in this study and their definitions.

Predictor	*Definitions*	*Pre-specified hypothesis*
Participant characteristics		
Age (years)	Mean age of the participants	Increasing age increases recruitment and retention [10,13,26,27]
Sex	Proportion of female participants	Higher proportion of female increases recruitment [20] and reduces retention [26,29]
Socio-economic status (SES)	Studies were labelled as low SES when the majority of the participants were described as having low education levels, low income, being unemployed, homeless, receiving government benefits, in prison, or sample otherwise labelled as 'low SES'	Low SES reduces recruitment [11] and reduces retention [28,38]
Nicotine dependency	Level of nicotine dependence as assessed on the Fagerström Test for Nicotine Dependence [46] Missing values were imputed based on cigarettes per day scores where available	Higher nicotine dependency reduces recruitment [11] and retention [6]
Motivation to quit	Motivation is assumed present when either one of the following two variables is yes: •Explicit inclusion criteria of intent to quit •Motivation as otherwise suggested in the individual studies	Higher motivation to quit increases recruitment [22] and retention [27,39]
Chronic illness	Presence of an ongoing physical health condition such as diabetes in the majority of the participants	Reduces recruitment and retention
Physical health trigger	Presence of a health-related trigger for smoking cessation, such as pregnancy or being hospitalized with cardiac condition, in the majority of the participants	Increases recruitment and retention
Mental health including substance use disorder	Presence of an ongoing mental health condition, including substance use disorders, in the majority of the participants	Reduces recruitment and increases retention
Recruitment and retention strategies		
Recruitment method	•Targeted methods focus on recruiting individuals who may be more likely to meet eligibility criteria and provides a more personal approach •Non-targeted recruitment efforts are broad based, reach a much larger population and are less personal •Direct recruitment involves direct contact with potential participants •Indirect recruitment involves public announcements through, for example, newspapers and radio •Combination of direct and indirect	Targeted and direct increases eligibility rates, recruitment rates [39] and retention rates

(*Continues*)

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Table 1. (Continued)

Predictor	*Definitions*	*Pre-specified hypothesis*
Financial incentives for sample collections	Use of financial incentive for providing biochemically verified outcomes	Increases retention [23] and differential retention
Trial characteristics		
Type of biochemically verified smoking cessation	•Cotinine •Carbon monoxide (CO) •Cotinine and CO	Cotinine and CO reduce retention
Primary end-point	If the time-point assessed is the primary time point as defined by the included studies	Increases retention and there is higher between groups retention in the primary end-point
Length of study follow-up	Length of study follow-up post-randomization in weeks [a]For differential retention model length of follow-up not included except as part of multi-level structure	Longer follow-ups reduce recruitment and retention. If there is a difference in retention rates between groups, this will increase over time
Intervention characteristics		
Mode of delivery of the intervention	•Individual (i.e. face-to-face) •Group (i.e. on a group basis) •Self-help (i.e. not individual). [a]Whether there was a higher level of mode of delivery in the intervention compared with the comparator group. Individual-level delivery was regarded as the highest level, followed by group delivery followed by self-help or no intervention	Individual increases recruitment and retention and differential retention
Number of BCTs for smoking cessation used in the intervention	Number of behavioural change techniques for smoking cessation (i.e. quitting and abstinent) used in the intervention [a]Difference in the number of BCTs for smoking cessation (intervention minus control group)	A higher number of quitting and abstinent BCTs increases retention and differential retention
Frequency of the intervention	Number of contact points for the intervention [a] Difference in number of contact points (intervention group minus comparator group)	Higher number of contact points decreases recruitment, retention and differential retention
Financial incentives for smoking cessation	Use of financial incentives for smoking cessation (e.g. incentives contingent on smoking abstinence)	Increases retention [14] and differential retention
Any financial incentive	Use of any financial incentives that is for smoking cessation and sample collection or intervention adherence	Increases recruitment [4]
Pharmacological support	Use of smoking cessation medication as part of the study [a]Whether pharmacological support was available in the intervention group only	Increases recruitment rate, retention rates and differential retention rates
Intervention setting		Inpatients increases recruitment, retention and differential retention

(*Continues*)

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Table 1. (Continued)

Predictor	*Definitions*	*Pre-specified hypothesis*
	•Inpatients (i.e. for patients living in a health facility such as hospitals) •Outpatient (i.e. for patients attending a health facility without staying overnight) •Community (i.e. for people in a non-health setting) [a]Whether there was a higher level of setting in the intervention group compared with the control group. Inpatient setting was regarded as the highest level, followed by outpatient and then community setting	
Adjuvant interventions	An intervention provided that was hypothesized by the individual study authors to either indirectly lead to smoking cessation (e.g. a physical activity intervention) and/or have benefits as an add-on to an existing smoking cessation programme (e.g. support for weight-gain concerns), and that was not captured by any of the other active content predictors [a]Whether adjuvant interventions were present only in the intervention group	Increases recruitment, retention and differential retention
BCTs to engage participants in the intervention	Number of specific behavioural change techniques to engage participants in the intervention [a]Difference in the number of BCTs for to engage participants in the interventions between treatment and comparator	Higher number of BCTs increases retention and differential retention

BCT = behavioural change techniques. [a]Definition used for differential retention model. CO = carbon monoxide.

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blinding of outcome assessment, incomplete outcome data, selective outcome reporting, contamination bias, inappropriate administration of the intervention and stop early/continue for benefit.

RESULTS

Demographics and descriptive data

A total of 172 studies with 89 639 participants were ultimately included. Thirty-two of these trials were captured by the updated search [Fig. 1 for the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram and Supporting information material including the list of studies included in the review as well as a flow-chart summarizing the recruitment and retention process]. The studies were performed in four continents and 20 countries: Europe [Denmark (k = 1), France (k = 2), Germany (k = 1), Netherlands (k = 4), Norway (k = 3), Spain (k = 4), Sweden (k = 1), Switzerland (k = 5), Turkey (k = 1), United Kingdom (k = 13)], Oceania [Australia (k = 7) and New Zealand (k = 1)], North America [United States (k = 111) and Canada (k = 7)] and Asia [China (k = 6), Hong Kong (k = 2), Japan (k = 1), South Korea (k = 1), Malaysia (k = 1) and Pakistan (k = 1)].

Risk of bias of the included studies

We present assessments of the risk of bias in the intervention effects in each RCT as general study level descriptors.

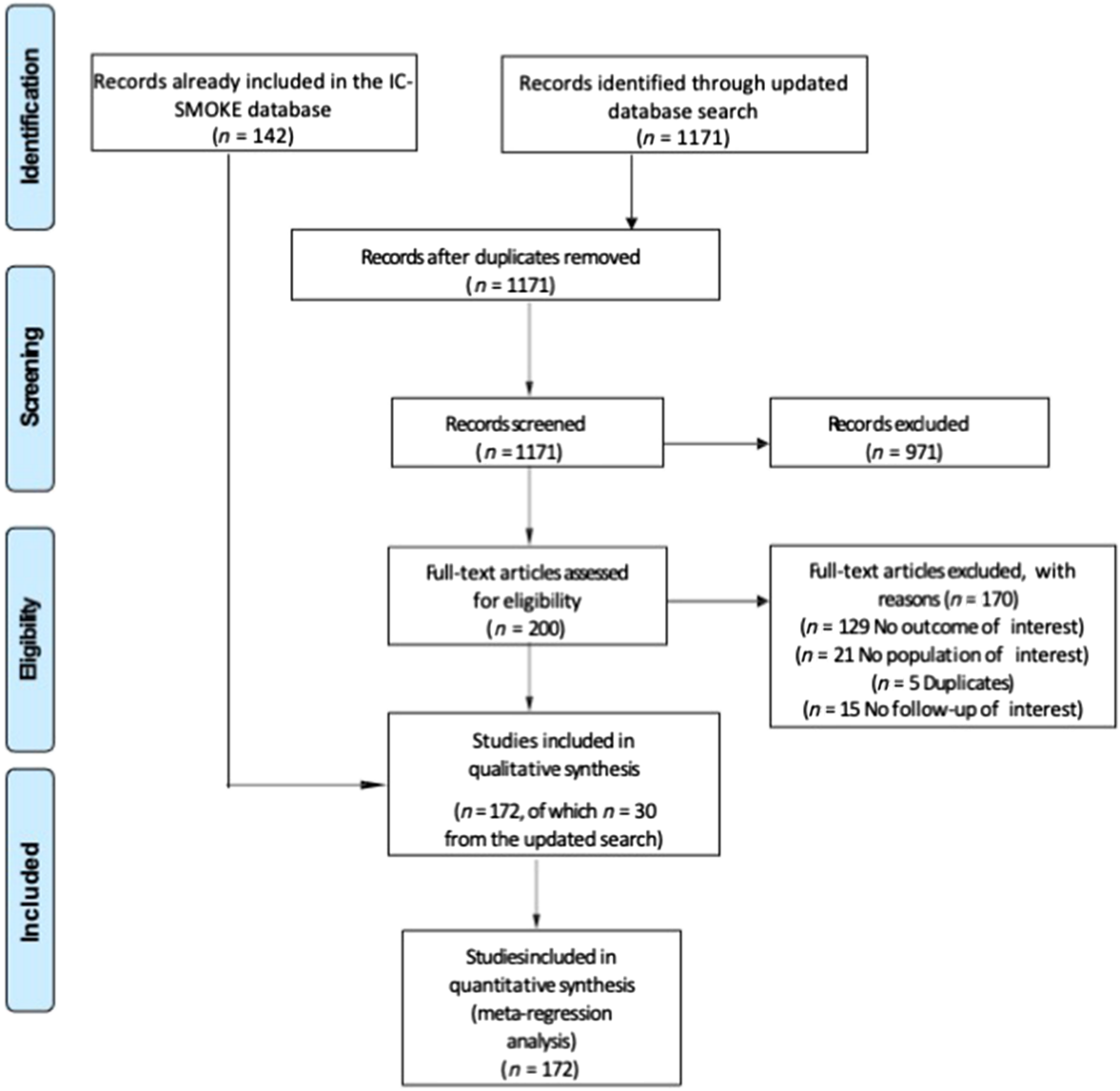

Figure 1 Flow-chart of the study selection process.

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We note, however, that risk of bias in the intervention effect does not necessarily translate to risk of bias in the outcomes in this review. Overall, 48 of 172 studies were judged as 'low risk of bias' in all the following items: selection bias, detection bias, attrition bias and reporting bias. All the trials were judged as being 'low risk of bias' for the 'blinding of outcome assessment' item, as the studies included biochemically verified smoking cessation outcomes. The table summarizing the risk of bias judgements is reported as Supporting information.

Participant characteristics

The median age of participants within the samples was 43.5 years [interquartile range (IQR) = 39.7–48.1], 49.2% were female (IQR = 37.4–60.0), 48 of 172 studies (28%) included most people with low socio-economic status and 77 of 172 (45%) included only people motivated to quit smoking. The median nicotine dependence of participants within the samples, assessed with the Fagerström Test for Nicotine Dependence, was 4.9 (IQR = 4.3–5.4). Twenty-seven (16%) and 25 (15%) included most people with an ongoing mental or physical condition, respectively. Thirty of 172 studies (17%) included most people who had experienced a health-related trigger for smoking cessation, such as pregnancy or being hospitalized with a cardiac condition.

Recruitment and retention strategies and trial characteristics

A targeted recruitment strategy (e.g. recruiting at a smoking cessation clinic rather than on the main street) was performed in 108 of 172 studies (63%). A direct recruitment strategy, which involves person-to-person contact with potential participants (e.g. an invitation from a health professional to take part in the study) was used in 92 of 172 (53%) studies, while 61 of 172 (35%) used an indirect approach (e.g. TV or radio advertisement) and 20 of 172 (12%) used both. The follow-up time ranged from 24 to 208 weeks (median = 52, IQR = 26–52).

Intervention and comparator characteristics

The mode of delivery of the intervention was individual [k = 119 (69%); i.e. one or more professionals deliver an intervention to a single participant, for example face-to-face, by video or on the telephone as long as it was delivered to one person at a time], in-group [k = 37 (22%); i.e. the intervention is delivered to a group of people all at the same time] or self-help [k = 17 (10%); i.e. does not involve a health professional but uses websites, books, leaflets and could be delivered to a single person or to groups]. The number of intervention sessions varied widely between one to 79 (median = 7.0, IQR = 3.0–10.5). Financial incentives for outcome sample collection or smoking cessation were used in 19 of 172 studies (11%) and 23 of 172 (14%), respectively. Pharmacological interventions were used in 115 of 172 studies (67%) and adjuvant interventions, such as weight loss or exercise interventions, were offered in 28 of 172 studies (16%). The setting where the intervention was delivered was inpatient [k = 12 (7%); i.e. for patients staying in a health facility such as hospitals], outpatient [k = 104 (60%); i.e. for patients attending a health facility without staying overnight] or in a community [k = 36 (21%); i.e. for people in a non-health setting]. The median number of BCTs used for quitting smoking and being abstinent was 13.0 (IQR = 5–25). Most of the comparator groups received an active intervention, such as medication only, self-help (leaflet, website), brief physician advice, individual counselling and group counselling. Very few comparators received were waiting-list controls.

Eligibility, recruitment and retention rates

A total of 137 (80%), 118 (69%) and 125 (73%) studies had complete data for the eligibility, recruitment and (differential) retention meta-regression models. The median eligibility, recruitment, retention and differential retention rates varied widely, and are reported in Table 2).

Table 2 Recruitment and retention rates for the included 172 studies.

Outcome	*Median*	*IQR*	*Range*
Eligibility rates[a] (k = 137)	57.6%	34.7–83.7%	1–100%
Recruitment rates[b] (k = 143)	66.4%	42.7–85.2%	8–100%
Retention rates[c] (k = 125)	80.5%	68.5–89.5%	10–100%
Differential retention rates[d] (k = 125)			
Intervention groups	80.1%	67.9–89.3%	10–100%
Comparator groups	81.1%	68.6–89.6%	22–100%

[a]Eligibility rates (number randomized + number declined/number assessed for eligibility). [b]Recruitment rates (number randomized/number eligible). [c]Retention rates (number providing biochemically verified outcomes/number randomized). [d]Differential retention rates (difference in number providing outcomes in the intervention group and number providing outcomes in the comparator group). IQR = interquartile range.

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Predictors of eligibility rates

There were no statistically significant associations between recruitment strategies and eligibility rates, defined as the proportion of people eligible out of the total screened for eligibility. Eligibility rates seemed higher in studies using a targeted recruitment strategy (versus a non-targeted recruitment strategy) (OR = 1.26, 95% CI = 0.59–2.72) and in studies using a combination of indirect and direct (OR = 1.72, 95% CI = 0.66–4.45) or only indirect recruitment strategy (OR = 1.99, 95% CI = 0.88–4.47, versus studies using a direct recruitment strategy, i.e. via a direct contact with potential participants). However, CIs were wide, making evidence for the association of these predictors with eligibility rates inconclusive.

Predictors of recruitment rates

Recruitment rates were lower in studies using an indirect recruitment strategy (versus direct contact with potential participants) (OR = 0.30, 95% CI = 0.11–0.82) and in studies using self-help smoking cessation interventions (versus individual, person-delivered interventions) (OR = 0.14, 95% CI = 0.03–0.67). There was no association between the other predictors included in this model and recruited rates (Table 3).

Table 3 Association between participant characteristics, recruitment and retention strategies, trial characteristics and intervention characteristics with recruitment and retention rates.

	Recruitment rates[a]				*Retention rates*[b]			
Predictor	*OR*	*Lower 95% CI*	*Upper 95% CI*	*P-value*	*OR*	*Low 95% CI*	*High 95% CI*	*P-value*
Participant characteristics								
Age (years)	1.03	0.99	1.08	0.14	1.00	0.98	1.02	0.93
Female %	0.57	0.12	2.75	0.48	0.83	0.71	0.98	0.03*
Low SES (yes versus no)	1.06	0.54	2.05	0.87	1.00	0.71	1.41	0.99
Nicotine dependency (yes versus no)	0.98	0.68	1.41	0.92	0.97	0.86	1.01	0.63
Motivation to quit (yes versus no)	1.28	0.69	2.38	0.43	0.74	0.55	0.99	0.04*
Ongoing physical condition (yes versus no)	0.50	0.20	1.25	0.14	1.66	1.04	2.63	0.03*
Ongoing mental condition (yes versus no)	1.95	0.74	5.14	0.18	0.90	0.56	1.44	0.65
Health trigger (yes versus no)	0.79	0.31	1.98	0.61	1.14	0.71	1.83	0.60
Recruitment and retention strategies								
Targeted versus non-targeted	0.37	0.16	0.87	0.22	0.74	0.48	1.14	0.18
Indirect versus direct	0.30	0.11	0.82	0.02*	0.60	0.38	0.97	0.04*
Direct + indirect versus direct	0.74	0.27	2.01	0.55	1.21	0.54	1.50	0.67
Any financial incentives (i.e. sample collection or smoking cessation or intervention adherence)[c] (yes versus no)	1.51	0.41	5.49	0.53	NA			
Financial incentives for sample collection (yes versus no)	NA				1.04	0.95	1.67	0.88
Trial characteristics								
Cotinine assessment versus CO assessment	NA				0.89	0.67	1.18	0.41
CO and cotinine assessment versus CO assessment	NA				0.90	0.70	1.14	0.37
Primary end-point	NA				1.00	0.93	1.09	0.92
Length of study follow-up	1.49	0.75	2.97	0.25	0.83	0.79	0.87	< 0.01*
Intervention characteristics								
Self-help intervention versus individual intervention	0.14	0.03	0.67	0.01*	1.12	0.93	1.34	0.25
Group-based intervention versus individual intervention	1.11	0.44	2.82	0.82	1.03	0.83	1.27	0.82
Number of sessions	0.74	0.49	1.11	0.14	1.00	0.93	1.08	0.98
Financial incentives for smoking cessation[c] (yes versus no)	NA				1.21	0.95	1.53	0.12
Pharmacological support (yes versus no)	0.60	0.29	1.25	0.17	1.14	0.99	1.32	0.08
Outpatient setting versus inpatient setting	0.91	0.26	3.21	0.88	0.94	0.50	1.77	0.85
Community setting versus inpatient setting	1.99	0.45	8.91	0.37	1.03	0.53	1.99	0.94
Adjuvant interventions (yes versus no)	1.21	0.47	3.11	0.69	0.94	0.76	1.16	0.55
Number of BCTs for smoking cessation	NA				1.00	0.99	1.01	0.68
Number of BCTs for engagement	NA				1.01	0.94	1.08	0.85

[a]Recruitment rates (no. randomized/no. eligible) [b]Retention rates (number providing outcomes/number randomized). [c]Financial incentives: financial incentives for sample collections (e.g. CO_2, cotinine) and financial incentives for smoking cessation have been merged into one predictor variable for the model on recruitment rates; BCT = behavioural change technique; NA = not assessed; OR = odds ratio; 95% CI = confidence interval; SES = socio-economic status; CO = carbon monoxide. *Statistically significant associations ($P < 0.05$); no. = reference category.

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Predictors of retention and differential retention rates

Retention rates were higher in studies including people with an ongoing physical condition (versus including people without an ongoing physical condition) (OR = 1.66, 95% CI = 1.04–2.63). By contrast, studies including a higher proportion of female participants (OR = 0.83, 95% CI = 0.71–0.98) and participants being motivated to quit (OR = 0.74, 95% CI = 0.55–0.99) reported lower retention rates. However, the 95% CIs were wide, and the results need to be interpreted with caution. Additionally, studies using an indirect recruitment method (versus a direct recruitment method) reported lower retention rates (OR = 0.60, 95% CI = 0.38–0.97), and the later the follow-up assessments, the lower were the retention rates observed (OR = 0.83, 95% CI = 0.79–0.87) (Table 3).

In the model predicting differential retention, there was evidence of a higher retention rate when there were financial incentives for smoking cessation in the intervention compared with the comparator group (OR = 1.35, 95% CI = 1.02–1.77) (Table 4). However, the 95% CIs were wide, and the results need to be interpreted with caution. There was no clear evidence for the association of other predictors on differential retention.

Sensitivity analysis

Including continent of origin of the study for eligibility, recruitment, retention showed that studies performed in North America (United States and Canada) compared to studies performed in Europe reported lower recruitment rates (OR = 0.33, 95% CI = 0.15–0.80). We found no association between continent of origin of the study and eligibility or retention rates (Supporting information, Tables S2, S3 and S4). The results of the subgroup analysis including only studies that tested an interpersonal smoking cessation behavioural intervention did not differ from the main analysis (Supporting information, Table S5).

DISCUSSION

To the best of our knowledge, this is the first review to quantify recruitment and retention rates in behavioural randomized controlled trials of smoking cessation interventions and to assess the associated factors. Average eligibility rates, recruitment rates and retention rates varied widely between trials, whereas differential retention rates were small. Several pre-specified sample, trial and intervention characteristics predicted trial recruitment and retention. Most notably, an indirect recruitment method (posters, website) predicted lower recruitment (of those eligible, fewer participated) and retention (of those randomized, fewer were retained) in the trial. Fewer eligible people agreed to be randomized to self-help interventions (compared to in-person delivered interventions) and retention was higher in interventions that contained financial incentives for smoking cessation. In terms of sample characteristics, studies conducted in the United States had lower trial recruitment, and trials with more women and people more motivated to quit smoking had lower retention rates. These results can be used to help estimate trial participant or design strategies for enhancing participation in future trials.

It is also important to note that many of the trial, participant and intervention characteristics that were hypothesized to predict trial participation did not do so. Many of these characteristics were identified in previous research, such as nicotine dependence [6] and age [10,13,26,27], but when examined across trials while controlling for the other variables in the model there was no evident association with trial participation. However, most associations were in the expected direction, but were either too small

Table 4 Predictors of differential retention.

	OR	*Lower 95% CI*	*Upper 95% CI*	*P-value*
Predictor				
Trial characteristics				
Primary end-point	1.11	0.95	1.29	0.20
Intervention characteristics				
Individual mode of delivery[a]	0.90	0.76	1.05	0.18
Difference in frequency[a]	1.14	0.97	1.34	0.11
Financial incentives for smoking cessation[a]	1.35	1.02	1.77	0.04[a]
Pharmacological support[a]	0.97	0.81	1.15	0.70
Inpatient setting[a]	0.95	0.70	1.29	0.74
Adjuvant therapy[a]	1.05	0.82	1.33	0.71
Difference in number of BCTs for smoking cessation[a]	1.00	0.99	1.00	0.39
Difference in number of BCTs for engagement[a]	1.00	0.94	1.07	0.97

[a]Intervention group minus comparator group or higher level in intervention group compared with control group. BCT = behavioural change technique; OR = odds ratio; 95% CI = confidence interval; SES = socio economic status. [*]Statistically significant associations ($P < 0.05$).

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or with too much uncertainty to reach a statistically significant association. Nevertheless, these estimates combined may allow those planning future smoking cessation trials to better estimate and manage participant recruitment and retention rates in their trial.

Results in context

Recruitment rates

Approaching adult smokers directly, i.e. via a direct contact with potential participants, may improve recruitment. This is in line with previous literature and our initial hypothesis, that if participants are approached by a health-care provider about the possibility of taking part in an RCT this increases the chances of the participants being randomized [35]. Also in line with our pre-specified hypothesis, testing self-help interventions, i.e. without an interpersonal contact, appears to discourage adult smokers from being randomized. This may be explained by the fact that people like an interaction with another person when possible, particularly when trying to stop smoking [36].

Retention rates

Our findings suggest that there may be a need to support retention in trials for women in particular. This confirms previous evidence [37]. Female adult smokers may have competing family responsibilities—such as having a child mdash;that interfere with their ability to meet trial participation demands or commitment to smoking cessation interventions [37,38].

A higher motivation to quit was associated with lower retention rates, contrary to findings in previous studies [39,40]. There are possible explanations for higher drop-out among those who are more motivated to quit. It may be because they quit and did not perceive added benefit in continuing with the trial [39]. Alternatively, they may feel a greater sense of guilt or failure if they continue smoking and therefore drop out.

The presence of an ongoing health condition such as diabetes or chronic obstructive pulmonary disease increases retention. This is in contrast with our initial hypothesis and with previous studies [11,39,41]. Perhaps this could be explained by the fact that people with a precarious health status may be more dedicated to persevering with the study to benefit from stopping smoking.

In line with our hypothesis, using a direct recruitment method may improve retention rates. People may have a 'closer' relationship with their physicians or recruiters, which make them feel more willing to continue participation [5,42]. This benefit should be balanced against ethical considerations such as coercion and dual relationships when deciding on recruitment methods. Additionally, still in line with our hypothesis, the longer the study follow-up assessments the lower the retention.

Financial incentives for smoking cessation promote higher retention. Studies providing financial incentives for smoking cessations in the intervention, but not to the comparator groups, had higher retention rates in these intervention groups. This is in line with our hypothesis and previous individual studies [43,44].

Implications for future research

Future studies testing behavioural interventions for smoking cessation may benefit from carefully planning participant trial participation. This study demonstrates that choices made to identify and recruit potential eligible people may ultimately also influence retention rates. It seems important to examine how women can be better supported to continue with trial participation and why men, who are the majority of smokers [45], were under-represented in smoking cessation studies, as were studies conducted in Africa and South America. Self-help interventions may benefit from some level of interaction in person (be it on-line or face-to-face), and this warrants further investigations. Incentives for smoking cessation may both motivate people to quit smoking [33] and complete the trial. With a longer follow-up, trialists may want to focus more resources on obtaining outcomes at the later follow-up time-points.

Finally, the results generated here may allow trialists to plan trial recruitment and retention rates more realistically and to enhance the chances of completing a well-powered trial within the time-frame set.

Strengths and limitations

A limitation of this study is the aggregate and observational nature of the data, so that causal relationships between the predictors and outcomes cannot be assumed. Secondly, trial participation data and participant recruitment methods were often poorly reported, which prevented us from running the analyses including all the studies available. Although we attempted to contact study authors to retrieve missing information, we received that information infrequently. This highlights the need to improve the reporting of the recruitment process in RCTs using behavioural interventions for smoking cessation. Finally, our search strategy dates to 2018; however, it is unlikely that drivers of trial participation have changed drastically since we performed the search.

Strengths of this study were that all models were pre-specified based on a literature review and expert input, and considering potential causes of confounding. A large number of trials and all available time-points were included. We were also able to examine the whole cascade

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from assessing eligibility to (differential) retention in the trial. This carefully designed study using a very large data set of smoking cessation trials thus allowed for identifying the factors associated with trial participation across trials, populations and countries, and factors that are proposed to be associated but did not show a relevant association in this meta-analysis.

CONCLUSIONS

Trial participation can vary substantially between trials and impact trial feasibility, internal validity and external validity. This meta-analysis using pre-registered analyses identified that in randomized controlled trials of behavioural smoking cessation interventions recruitment and retention rates appear to be higher for smoking cessation interventions that include a person-to-person rather than at-a-distance contact; male participants, smokers with chronic conditions, smokers not initially motivated to quit and shorter follow-up assessments seem to be associated with improved retention; financial incentive interventions improve retention in groups receiving them relative to comparison groups. This knowledge could improve planning and management of future smoking cessation trials.

Study registration

PROSPERO CRD42019121453, and https://osf.io/5er49/

Declaration of interests

None.

Acknowledgements

This work was funded by Cancer Research UK (application number C50862/A25405). The funder had no role in protocol design, decision to publish, or preparation of the manuscript.

Author contributions

Alessio Bricca: Conceptualization; data curation; formal analysis; methodology. **Zoe Swithenbank:** Conceptualization; data curation; investigation. **Neil Scott:** Conceptualization; data curation; formal analysis. **Shaun Treweek :** Conceptualization; methodology. **Marie Johnston:** Conceptualization; supervision. **Nicola Black:** Conceptualization; formal analysis; software. **Jamie Hartmann-Boyce:** Conceptualization. **Robert West:** Conceptualization. **Susan Michie:** Conceptualization. **Marijn de Bruin:** Conceptualization; formal analysis; funding acquisition; project administration; supervision.

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