Full title: Effectiveness and cost-effectiveness of behavioural support for prolonged abstinence for smokers wishing to reduce but not quit: Randomised controlled Trial of physical Activity assisted Reduction of Smoking (TARS).

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Declaration of interests

SC reports that Peninsula Clinical Trials Unit received NIHR CTU support funding for the duration of this trial. Prof Creanor declares that she was Chair of the NIHR Research for Patient Benefit South West Advisory Committee from May 2017 to April 2021, outside the submitted work.

TH declares membership of the NIHR HTA Primary Care and Community Preventive Interventions Prioritisation Committee and subsequently the HTA Prioritisation Committee A from 2016-2019

CGree declares the following committee membership: HTA General Committee 01/03/2019 until 02/10/2020.,

LP received funding from the trial grant as a consultant while at the University of Exeter, as part of the physical activity and health across the lifespan group (within sport and health sciences department), is part of a collaboration with Activinsights, the manufacturer of the GENEActiv accelerometer used within this trial. The collaboration provides data analytics services for human activity research.

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# **Abstract**

## Aims

For smokers unmotivated to quit, we assessed the effectiveness and cost-effectiveness of behavioural support to reduce smoking and increase physical activity on prolonged abstinence and related outcomes.

## Design

A multi-centred pragmatic two-arm parallel randomised controlled trial.

Setting

Primary care and the community across 4 UK sites.

Participants

915 adult smokers (55% female, 85% white), recruited via primary and secondary care, and the community, who wished to reduce their smoking, but not quit.

## Interventions

## Participants were randomised to support as usual (SAU)(n=458) versus multi-component community-based behavioural support (n=457), involving up to 8 weekly person-centred face-to-face or phone sessions with additional 6-week support for those wishing to quit. Measurements

## Ideally, cessation follows smoking reduction so the primary pre-defined outcome was biochemically-verified 6-month prolonged abstinence (from 3 to 9 months, with a secondary endpoint also considering abstinence between 9 and 15 months).Secondary outcomes included biochemically-verified 12-month prolonged abstinence, and point prevalent biochemically-verified and self-reported abstinence, quit attempts, number of cigarettes smoked, pharmacological aids used, SF12, EQ-5D, and moderate-to-vigorous physical activity (MVPA) at 3 and 9 months. Intervention costs were assessed for a cost-effectiveness analysis.

## Findings

Assuming missing data at follow-up implied continued smoking, nine (2.0%) intervention and four (0.9%) SAU participants achieved the primary outcome (adjusted odds ratio 2.30, 95% confidence interval (CI): 0.70 to 7.56, p = 0.169). At 3 and 9 months the proportions self-reporting reducing cigarettes smoked from baseline by ≥50%, for intervention versus SAU, were 18.9% v 10.5% (p = 0.009), and 14.4% v 10% (p = 0.044), respectively. Mean difference in weekly MVPA at 3 months was 81.6 minutes in favour of the intervention group (95% CI: 28.75, 134.47: p = 0.003) but there was no significant difference at 9 months (23.70, 95% CI: -33.07, 80.47: p=0.143). Changes in MVPA did not mediate changes in smoking outcomes. The intervention cost was £239.18 per person, with no evidence of cost-effectiveness.

## Conclusions

For UK smokers wanting to reduce but not quit smoking, behavioural support to reduce smoking and increase physical activity improved some short-term smoking cessation and reduction outcomes and moderate-to-vigorous physical activity but had no long-term effects on smoking cessation or physical activity.

Keywords: Smoking cessation, smoking reduction, prolonged abstinence, biochemical verification, behavioural support, physical activity, motivational interviewing, multiple behaviour change, health economic evaluation

**INTRODUCTION**

## For people attempting to stop smoking, a combination of pharmacotherapy and behavioural support maximises the likelihood of cessation. 1-3 Such interventions are highly cost-effective and, consequently, guidelines recommend that health systems provide such care and people take-up the offer. 4

## For smokers wishing to reduce but not immediately quit, the effects of tobacco harm reduction interventions on abstinence are less certain and healthcare professionals and policy makers urgently seek evidence-based guidance. Two systematic reviews show evidence that nicotine replacement therapy (NRT), often with behavioural support, can reduce smoking and increase quit attempts and abstinence for smokers not immediately wishing to quit. 5, 6 However, a significant proportion of smokers do not wish to use pharmacological aids, including e-cigarettes and licenced nicotine containing products (LNCPs) for several reasons, including the uncertainty of health risks. 7

Prior to the present study we identified four RCTs 8-11 that examined the effects of behavioural support for smoking reduction among smokers wishing to reduce smoking but not quit. Our unpublished meta-analysis of intervention effects on the most rigorous outcomes in these studies provided a pooled relative risk (RR) of abstinence of 1.46 (95% CI: 0.90 to 2.38), suggesting that such interventions are effective for increasing quit attempts and point prevalence abstinence; however, there was a high risk of bias, with only one study biochemically-verifying abstinence 11 and none assessing floating prolonged abstinence. 12

Continued smoking by people with moderate to high tobacco dependence who want to reduce but not quit is usually driven by urges to smoke or cravings. 13 There is strong evidence that the intensity of these urges can be acutely reduced by physical activity. 14 For smokers wishing to quit, a systematic review of exercise interventions provided little evidence for physical activity aiding sustained smoking cessation. 15 However, most trials were of low quality, and comparisons were mostly with existing evidence-based effective treatments which possibly minimised any effects.

In a pilot RCT we uniquely examined the acceptability, feasibility, intervention fidelity and exploratory effectiveness of behavioural motivational support to promote smoking reduction and physical activity among smokers who wished to reduce their smoking but not quit. 16-18 Intervention participants were twice as likely to reduce their self-reported smoking by at least fifty percent, were nearly four times more likely to attempt to quit, and two to three times more likely to be biochemically-verified as abstinent in the short-term. Participants appreciated the value of physical activity as a diversionary shift to a more positive health identity, for managing mood and weight gain, and the intervention was plausibly cost-effective. The pilot also highlighted the need to embrace a flexible approach to supporting disadvantaged smokers, who wished to reduce in different ways and timescales, and offer evidence-based support when they wished to quit, aligned to a Phase-Based Model. 19

The present study (Trial of physical Activity assisted Reduction of Smoking; TARS) aimed to test the effectiveness and cost-effectiveness of a multi-component intervention for smokers wishing to reduce but not quit, to increase biochemically-verified, 6-month prolonged abstinence, and other smoking and physical activity outcomes, while seeking to understand the role of the respective components.

## **METHODS**

**Study design and participants**

We conducted a pragmatic, multi-centred, parallel two-arm, community-based, randomised controlled, superiority trial. The published protocol describes the trial procedures in detail. 20

We recruited participants from UK primary and secondary care and community settings using a wide range of methods including GP letters, text messages and e-mails, community adverts and social media, at four sites: East Midlands; South Central England; Devon and Cornwall; and London. After expressing interest, potential participants were screened by phone. Participants were aged ≥18 years, smoking ≥10 cigarettes per day (for at least 1 year), wishing to reduce smoking, but not quit immediately. They were ineligible if unable to engage in at least 15 minutes of continuous moderate intensity physical activity, had illness or injury that might be exacerbated by exercise, or were unable to engage in the study and/or intervention due to language or other reasons. We did not exclude those who also wished to use pharmacological aids but accounted for this in our analysis plan. Participants gave written informed consent.

The study was approved by the South West Central Bristol Research Ethics Committee (REC reference: 17/SW/0223) and Health Research Authority and registered with the International Standard Randomised Controlled Trial Number register (ISRCTN47776579) prior to trial commencement. An independent Trial Steering Committee and Data Monitoring Committee oversaw the trial.

**Randomisation and masking**

Following baseline assessments, participants were randomised by the Peninsula Clinical Trials Unit (CTU) using a web-based system to conceal allocation. Participants were individually randomised to intervention or support as usual (SAU) group (1:1 ratio) using random permuted blocks, with stratification by recruitment site and the Heaviness of Smoking Index (HSI) 21 (low versus high) as a measure of dependence. An independent statistician developed the sequence.

Participant blinding was not possible. Researchers conducting follow-up assessments were masked to participants’ allocation, and primary analysis of primary and secondary outcomes was undertaken by trial statisticians blinded to allocation. We also used objective biochemically-verified abstinence.

**Procedures**

Briefly, intervention participants were offered up to eight, usually weekly, behavioural support sessions, face-to-face or by phone, lasting 10-60 minutes, to reduce smoking and increase physical activity, as described in detail elsewhere. 20 Up to six additional cessation-support sessions were offered to participants who decided to make a quit attempt. Building on the pilot study 16 and patient and public involvement, an intervention manual underpinned training (see: <http://hdl.handle.net/10026.1/17035>) and supervision of eight health trainers (two per site) with experience of delivering behaviour change interventions, and was the basis for the assessment of intervention fidelity. The client-centred intervention, particularly designed to engage with those living in disadvantaged communities, was informed by motivational interviewing and Self-Determination Theory. 22 The TARs intervention aimed to enhance participant’s sense of importance and confidence to autonomously change behaviours while connecting with others. The content had some overlap with interventions with a focus on smoking reduction for those smokers unmotivated to quit (8-11). Participants were encouraged to self-monitor and set goals for both smoking and physical activity, problem solve to overcome barriers for changing both behaviours, identify links between how physical activity may influence smoking acutely and chronically and vice versa, and to manage social influences that influenced the two behaviours. For example, with personal experimentation we encouraged participants to use physical activity to manage cravings and weight gain, and shift to a healthier self-identity. For participants wishing to quit, additional health trainer support sessions were provided to help maintain abstinence and to also access support as usual.

Support as usual (SAU) participants received brief advice on smoking cessation immediately post-randomisation, reflecting guidelines in the UK for smokers not wishing to quit, (see Appendix 1).

Baseline data, including demographics and smoking and physical activity history were collected in-person or by telephone. Follow-up data were collected by telephone or mailed survey. At 3 and 9 months, participants who reported making a quit attempt and having not smoked were asked to complete a biochemical-verification of abstinence. At 15 months, only those with biochemically-verified abstinence at 9 months were followed up to determine 12-month prolonged abstinence (i.e., 3 to 15 months) and identify any additional participants who achieved 6-month prolonged abstinence from 9 to 15 months.

**Outcomes**

To extend the evidence for sustained intervention effects the primary outcome was floating (i.e., no fixed quit date) biochemically-verified 6-month prolonged smoking abstinence (as recommended by Aveyard and colleagues 12) between 3 and 9 months, biochemically-verified using a CareFusion MicroCO meter (Williams Medical Supplies, Rhymney, UK, [www.carefusion.co.uk](http://www.carefusion.co.uk)). Due to COVID-19 related restrictions introduced on March 26th, 2020 in the UK, two of 48 participants at 9 months, and nine of 21 participants at 15 months, were provided with a mailed saliva cotinine test kit (ABS Laboratories, York, UK, [www.acmgloballab.com](http://www.acmgloballab.com)). At 3 months, participants who reported making a quit attempt (at least 24 hours without a puff) since joining the study, smoking not a puff since the quit date and providing an exhaled CO<10ppm, were deemed abstinent. At 9 months, participants who had been confirmed as biochemically-verified abstinent at 3 months and who reported having smoked fewer than five cigarettes since that quit attempt, were deemed abstinent with biochemically-verification.

Secondary smoking outcomes were floating 12-month prolonged, biochemically-verified smoking abstinence (between 3 and 15 months), and point prevalence self-reported abstinence, cigarettes per day, biochemically-verified abstinence and quit attempts at both 3 and 9 months. Use of e-cigarettes or LNCPs and urge and strength of urge to smoke 23 were self-reported at 3 and 9 months. The proportion of participants reducing the number of cigarettes smoked by ≥50% between baseline and 3 and 9 months was also determined. For analyses of smoking abstinence outcomes, non-responders were assumed to be smoking. 24 Also assessed were self-reported seven-day physical activity recall 25 (at 3 and 9 months) and GENEActiv accelerometer (only at 3 months for a sample of participants) recorded moderate-to-vigorous physical activity (MVPA), and self-reported body mass index, sleep, and quality of life (SF-12, EQ-5D-5L), 26, 27 (at 3 and 9 months).

For the trial-based cost-effectiveness analysis, we estimated the direct cost of delivering the intervention from contact data collected during the study by health trainers and based on assumptions and estimates provided by investigators for cost components not measured during the study. We estimated Quality Adjusted Life Years (QALYs) from participant-reported EQ-5D-5L (mapped to EQ-5D-3L value set) 26 and costs from a health and social care resource use questionnaire, completed at baseline, 3 and 9 months.

Serious adverse events (SAEs), defined as a hospitalisation or sudden death, were recorded during the trial up to 8 weeks after the 9-month follow-up and were assessed for likelihood of relatedness to the trial procedures.

**Statistical analysis**

We aimed to recruit 900 participants, giving 90% power at the two-sided 5% significance level to assess whether the intervention increased the biochemically-verified 6-month prolonged smoking abstinence rate from 5% in the control group to 11%. These estimated abstinence rates were consistent with the pilot study 16 and those in a systematic review of pharmacological interventions. 28 As only participants who were unavoidably lost to follow-up (death or address untraceable) were excluded from the primary analysis (expected to be <5% of recruited participants), the sample size was not inflated for loss to follow-up.

A detailed study protocol (finalised 11th June, 2020), statistical analysis plan (finalised 20th September, 2020) and health economic evaluation plan (finalised 5th November, 2019) were approved by the oversight committees prior to locking the trial database and are available at <https://fundingawards.nihr.ac.uk/award/15/111/01>. 29

Primary analyses of primary and secondary outcomes, and reported SAEs, were by intention-to-treat (ITT). Analyses employed Stata 14.0 and R4.0.3; the inferential analyses were pre-specified in the statistical analysis plan, for which the primary analysis was independently programmed by two statisticians.

Fully adjusted models included the stratification variables (site and HSI), as well as the corresponding baseline measure of outcome being modelled, where appropriate. Adjustments for multiple analyses were not made. 29 To check that the intervention effect was not heterogeneous across study centres we tested the interaction between intervention and study site using a fixed-effect model. There was no evidence for this (p-value = 0.8338) and consequently the inclusion of a random effect term for site was not necessary in our analysis model.

The primary analysis of the primary outcome used a multi-variable logistic regression model to compare the floating biochemically-verified 6-month (between 3 and 9 months) prolonged abstinence rate, between groups, with adjustment for stratification factors. Both adjusted and unadjusted odds ratios (ORs) and 95% CIs were determined, together with absolute between-group differences. Intervention effectiveness was also presented as a relative risk, calculated from the estimated OR for the intervention and the baseline rate for the SAU group, along with the corresponding 95% CI. Planned sensitivity analyses of the primary outcome included a “best-case scenario”, where participants with missing primary outcome data were assumed to have quit at 3 and 9 months, and a complier average causal effect (CACE) analysis to determine intervention effects for participants who had received a pre-determined dose of at least two interventions sessions, compared with those who received fewer and SAU participants. Additional planned analyses included adjustment for potential confounding variables at baseline (Index of Multiple Deprivation (IMD), self-reported MVPA, LNCP use, vaping), in addition to the stratification factors, if there were notable group imbalances at baseline. An exploratory analysis of the health trainer effect using a multi-level, mixed-modelling approach to allow for the partially nested data (participants allocated to the intervention group were partially clustered within the HT, in turn nested within sites) was also planned. To test the significance of adding an interaction between allocated group and study centre, the log-likelihood from the interaction model was compared to that from the primary model of the primary outcome fitted to the same data subset (N=761).

The analyses of secondary outcomes followed a similar approach to that for the primary outcome, using both adjusted and unadjusted multi-variable logistic or linear regression modelling, and pre-planned exploratory analyses as for the primary outcome.

We were unable to test the mediating effects of PA on the primary outcome due to sparsity of data but we did explore if intervention effects on self-reported PA at 3 months mediated effects on cigarettes smoked and % achieving ≥ 50% smoking reduction from baseline to 3 and 9 months (see Figure 1). We used structural equation modelling (SEM) 30 with confidence intervals for the mediated path estimated through the bootstrap resampling method, with 1000 replications.

The cost-effectiveness analysis included only complete cases, i.e., participants for whom we could calculate a total cost and QALYs over 9 months and for whom we had full baseline data. A generalised linear modelling approach was used, with adjustment for baseline costs and quality of life.

## **RESULTS**

The flow of participants is shown in Figure 2. Between January 15th 2018 – 6th June 2019, 1441 people were screened, of whom 915 (63%) were eligible, consented and randomly assigned to the intervention (n=457) or SAU (n=458). Six-hundred and forty-nine (71%) were recruited via primary care, predominantly after a search of medical records and mailed, e-mailed or texted an invitation, with the remainder through secondary care, various community and social media engagement. The last follow-up was on 20th August 2020.

Participants’ baseline characteristics are shown in Table 1 and were balanced across groups. Approximately 60% came from postcodes in the 40% most deprived areas of England, with 17% unemployed, and 21.5% having no qualifications. The mean (SD) age was 49.8 (13.9) years, 55.4% were female, and most identified as white (84.9%). Overall, 30.3% reported having a partner who smoked. Participants smoked a mean (SD) of 18.0 (13.4) daily cigarettes with 32.6% smoking within 5 minutes of waking. No participants reported using a pharmacological smoking cessation product, 11% used vaping and 7% used LNCPs. Participants reported a greater perceived importance of and confidence for reducing rather than quitting smoking. Follow-up of participants is detailed in Figure 2. In summary, 318/457 (69.6%) intervention participants and 306/458 (66.8%) SAU participants completed the 3-month questionnaire and 298/457 (65.2%) and 285/458 (62.2%) completed the 9-month questionnaire. There was no evidence of differential follow-up rates at either 3-month (95% CI: -3.3% to 8.8%; p=0.368) or 9-month (95% CI: -3.2% to 9.2%; p=0.348) follow-up. Only participants with biochemically verified abstinence at 9 months were scheduled for 15-month follow-up; 20/26 (76.9%) intervention group and 19/22 (86.4%) SAU group were successfully followed-up at 15 months.

Intervention participants had a mean (SD) 4.8 (3.4) sessions with a health trainer which lasted a mean (SD) of 33.5 (20.3) minutes. Overall, the same proportion of sessions were delivered face-to-face and by phone, with the face-to-face sessions lasting over twice the duration of phone sessions. Seventy-six percent of intervention participants had ≥2 sessions.

The primary analysis included 450 (98.5%) intervention and 451 (98.5%) SAU participants as shown in Table 2. There was no significant between-group difference in primary outcome rates (2.0% (n=9) vs 0.9% (n=4)) in intervention and SAU, respectively; adjusted OR for biochemically-verified floating 6-month prolonged abstinence between 3 and 9 months, 2.30 (95% CI: 0.70 to 7.56); p=0.17). Most pre-planned sensitivity analyses were not conducted due to sparseness in data for the primary outcome, but of those able to be completed, none changed the findings of the main analysis. Applying the pre-specified best-case scenario to the primary outcome, the direction of effect switched to favouring the SAU group, with 27.5% of participants (n=124) categorised as being floating biochemically-verified 6-month prolonged abstainers in the SAU group compared with 24.2% (n=109) in the intervention group (OR 0.84, 95% CI: 0.62 to 1.14; p=0.26).

Seven serious adverse events were reported, five in the intervention and two in the control arm. None were deemed to be related to the intervention or to taking part in the study as shown in Appendix 2.

All nine participants in the intervention group who achieved the primary outcome attended at least two HT sessions. Secondary analysis of the primary outcome (i.e., combining those who achieved prolonged biochemically-verified 6-month prolonged abstinence between 3 and 9 months or between 9 and 15 months) showed no significant benefit from the intervention. Analysis of biochemically-verified 12-month prolonged abstinence (between 3 and 15 months) also showed no significant between group differences (see Table 2).

Results of the analysis of the smoking-related secondary outcomes are shown in Table 3. Marginal effects in favour of the intervention were evident at 3 months for both self-reported abstinence and biochemically-verified abstinence. There was no significant intervention effect on point prevalent self-reported and biochemically-verified abstinence at 9 months or at 15 months (only assessed amongst participants with verified abstinence at 9 months). On average, the intervention group reported smoking significantly fewer daily cigarettes than the control group at 3 months, but not at 9 months. A significantly greater proportion of intervention participants compared to SAU participants reported reducing daily cigarettes smoked by ≥50%, at both 3 months and 9 months. There was no significant between-group difference in the proportions reporting a quit attempt by 3 or 9 months.

At 3 months, the intervention group reported doing significantly more MVPA than the control group by 82 minutes per week but there was no significant difference in accelerometer recorded MVPA, for the sub-sample wearing them, as shown in Table 4. There were no significant between-group differences in BMI or self-reported daily average time spent sleeping in past week, at 3 or 9 months.

There was no evidence that the intervention effects on secondary outcomes differed by socio-economic status, baseline HSI, confidence in quitting or physical activity, or whether participants used medication or vaped during the study, or by centre, but analyses were limited by the number of participants involved.

From a low baseline reported use of vaping and LNCPs, at 3 and 9 months (assuming those who were missing at follow-up were not vaping or using LNCPs) the proportion vaping had approximately doubled at 3 and 9 months whereas the proportion using LNCPs remained similar at about 13-14% at 3 and 9 months, with no statistical differences between the groups. Given the non-significant findings and sparse data for the primary outcome we did not explore if change in vaping and/or LNCP usage mediated intervention effects on the primary outcome as planned.

As shown in Table 5 there was no evidence from the mediation analysis that intervention effects on self-reported MVPA at 3 months mediated changes in intervention effects on cigarettes smoked at 3 and 9 months or on the percentage of participants who reduced smoking by ≥50% from baseline to 3 or 9 months.

The estimated direct cost of delivering the intervention was £239.18 per participant, with sensitivity analyses ranging between £204 and £292. Four hundred and seventy participants (51.4%) contributed to the trial-based cost-effectiveness analysis, in which we estimated the intervention would lead to a non-statistically significant increase in costs (combining the cost of delivering TARS with the impact on NHS/PSS resource use) of £173.50 (95% CI: −£353.82 to £513.77) and a non-statistically significant decrease in QALYs of 0.006 (95% CI: 0.033 QALY decrease to 0.021 QALY increase), compared with SAU. Using central estimates, the intervention was dominated (more expensive and less effective than) by SAU. Considering sampling uncertainty, the probability that behavioural support was cost-effective over the 9-month trial duration was estimated to be 17% at a threshold of £20,000 per QALY, rising to 20% at a threshold of £30,000 per QALY. Numerous sensitivity analyses were conducted, including a multiple imputation analysis for missing data. These will be presented elsewhere. 31

## **DISCUSSION**

In people wishing to reduce but not immediately quit smoking, there was evidence that behavioural support to reduce smoking and increase physical activity levels can have short term effects on various smoking outcomes and physical activity but not increase biochemically-verified prolonged abstinence. Overall abstinence rates were much lower than expected, reducing the statistical power to exclude small differences in effectiveness, and too small to conduct analyses of the moderating effects of various baseline measures, or the mediating effects of physical activity on the primary outcome. Cost-effectiveness analysis suggested this intervention was not cost-effective in terms of driving quality of life gains within the trial follow-up window of 9 months.

The present findings add rigorous evidence to the few studies (with a high risk of bias), that have investigated the effectiveness of behavioural support for smokers wishing to reduce but not quit (predominantly without pharmacological support). 8-11 Our study involved similar delivery approaches to those reported across four identified studies (i.e., phone and face to face support for graduated reduction) and behaviour change components but involved generally greater intensity (i.e., more sessions), a more client-centred motivational interviewing approach (to maximise engagement with participants from disadvantaged communities) and a focus on multiple behaviour change.

Like previous behavioural support studies for smokers unmotivated to quit the present study showed some encouraging short-term intervention effects on point prevalent self-reported and biochemically verified abstinence but uniquely did not show that these effects could be sustained as evidenced by our primary outcome measure; floating 6-month prolonged biochemically verified abstinence. Such a measure may be a better predictor of permanent abstinence and hence health benefits and for assessing cost-effectiveness. The present study therefore challenges future studies on the effects of behavioural support (focusing on smoking and/or physical activity) to demonstrate more sustained abstinence for smokers initially unmotivated to quit.

In the present study, the percentage of participants in both arms of the trial using vapes and/or LNCPs doubled or tripled from baseline, depending on assumptions about missing data. At the time of our pilot study 16 use of such products were nowhere near as common and we were able to exclude smokers from the study who wished to use them and focus on promoting physical activity to support smoking reduction. It may be that an increase in participants vaping in both arms of the present trial washed out any effects of physical activity that were more evident in our pilot trial. Although the present study showed short-term intervention effects on physical activity we found no evidence that such effects mediated intervention effects of smoking outcomes, although we were limited by sparseness of data for some analyses.

To isolate the effective intervention components on respective smoking outcomes, the findings from three factorial studies have also been reported. 32-35 Across the three studies there was only very limited evidence of the beneficial effects of behavioural support and in some cases adding such support to pharmacological components reduced effectiveness, making the overall findings hard to interpret. Factorial studies which assign participants who are unmotivated to quit do not easily compare with the present pragmatic study involving a participant-centred approach with autonomy to use physical activity, vaping or LNCPs to manage cigarette cravings and smoking behaviour.

Our study widens the literature on the effects of physical activity on smoking outcomes. Most studies have examined the effects of structured exercise sessions on smoking cessation 15 for smokers who wish to quit while our focus was on behavioural support for those unmotivated to quit. On average, the TARS participants, like in our pilot trial, 16 were fairly active, reflecting a large proportion of participants living in areas with high social deprivation with low car ownership, physically active occupations and limited involvement in physically active leisure. While the intervention resulted in short-term increases in MVPA, these did not mediate changes in secondary smoking outcomes at 3 or 9 months. Our process evaluation, reported elsewhere, indicated that some interviewed participants embraced the idea of using physical activity to manage cravings, shift to a more positive health identity and manage weight gain due to smoking cessation, but other participants reduced their smoking without being more physically active (see 31).

Strengths of the present study include the large sample (relative to other studies 8-11, 16) of moderately heavy smokers initially unmotivated to quit and with low use of pharmacological aids to manage smoking, drawn from multiple sites with high social deprivation s. The intervention was evidence-based, participant-centred with good participant engagement. This is the first study to add physical activity promotion as part of behavioural support for reduction, and our extensive process evaluation provided valuable insights into processes of multiple health behaviour change.31 Further strengths were the use of stratified randomisation, researcher blinding for follow-ups, biochemical-verification of abstinence, and transparent, planned statistical and health economic analysis.

There were limitations. The low rate of floating prolonged abstinence was unexpected and undermined power to detect the relative difference in quit rates we expected, and planned sensitivity and secondary analyses of the primary outcome, including the moderation analysis. Despite this, we were able to exclude absolute differences in quit rate of the size we deemed a priori to be of clinical significance. Around a third of participants were not available for follow-up at 9 months. However, none of these people were abstinent at 3 months, meaning they could not have achieved the primary outcome. Some participants reported that they would have valued more flexibility, allowing longer intervals between support sessions and a longer time in which to reduce their smoking level, especially with improvements in respiratory function from becoming more physically active. 36

Future studies could explore the role of longer interventions and follow-up periods, especially since abstinence may be the result of multiple quit attempts, and more intensive interventions. 1 There is also a need to further examine psychological mediating processes (e.g., perceived importance and confidence to reduce and quit) identified in the TAR’s logic model as initially described elsewhere 31.

The health economic analysis showed a low probability that behavioural support for smokers who wished to reduce but not quit was cost-effective over the 9-month time horizon. This analysis included any benefits accruing due to the intervention detectable by a generic health-related quality of life questionnaire and was not restricted to benefits from changes in smoking behaviour but was limited due to substantial missing data and the short time horizon.

In summary, there was no evidence of intervention effectiveness on sustained abstinence, or that the TARS intervention was cost-effective. The TARS intervention achieved high engagement with predominantly socially disadvantaged moderately heavy smokers and its initial goals of supporting smoking reduction and increasing physical activity, but evidence is needed on how to convert these short-term benefits into sustained abstinence.

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Figure 1 Path model for mediating effects of changes in moderate to vigorous physical activity on smoking outcomes

Change in MVPA from 0-3 months

Intervention

C

B

A

Smoking outcomes at 3 and 9 months

Figure 2: Trial profile



\*Primary analysis of the primary outcome in line with the Russell Standard (i.e., participants with missing responses were considered to still be smokers with the exception of those unavoidably lost to follow-up, defined as participants who had died or were untraceable).

# Only participants with 9 month biochemically-verified abstinence were followed up at 15 months

Table 1: Baseline characteristics, according to study group. Values are numbers (percentages) unless stated otherwise

|  |  |  |
| --- | --- | --- |
|  | Intervention | Support as usual |
| **N** | 457 | 458 |
| Age (years) – mean (SD)  | 49.5 (14.1)  | 50.0 (13.6)  |
| Gender, female | 244 (53.4) | 263 (57.4) |
| Ethnicity, white  | 387 (84.7) | 390 (85.2) |
| Index of multiple deprivation rank a(derived from postcode) – mean (SD) | 14393.1 (8823.2) | 14467.6 (8655.3)  |
| Relationship status | Single (never married or civil partnered) | 200 (43.8) | 190 (41.5) |
| Married (or common-law partner) | 186 (40.7) | 197 (43.0) |
| Divorced or civil partnership dissolved | 54 (11.8) | 57 (12.4) |
| Other | 16 (3.5) | 14 (3.1) |
| Work situation | Working full or part-time in paid employment | 206 (45.1) | 212 (46.3) |
| In full time education | 21 (4.6) | 14 (3.1) |
| Retired | 70 (15.3) | 76 (16.6) |
| Unemployed | 83 (18.2) | 73 (15.9) |
| Other | 77 (16.8) | 83 (18.2) |
| Educational attainment  | No qualifications | 102 (22.3) | 95 (20.7) |
| First degree | 83 (18.2) | 104 (22.7) |
| Total daily equivalent cigarettes smoked – mean (SD) | 18.2 (13.2) | 17.4 (9.9) |
| Smoking more than 20 cigarettes per day | 125 (27.4) | 127 (27.7) |
| Smoking within 5 minutes of waking | 149 (32.6) | 149 (32.5) |
| Partner smokes, yes | 145 (31.7) | 132 (28.8) |
| Use vaping or licenced nicotine containing products, yes | 69 (15.1) | 59 (12.9) |
| Body mass index (Kg/m2) – mean (SD) | 26.4 (5.8) | 26.4 (5.8) |
| Weight (Kg) – mean (SD) | 76.7 (18.7) | 76.4 (19.2) |
| Self-reported total weekly minutes of moderate-to-vigorous PA – mean (SD) | 456.1 (434.0) | 462.4 (419.2) |
| Self-reported daily hours spent sleeping – mean (SD) | 6.9 (1.6)  | 6.7 (1.5)  |
| Important I reduce my smoking b | 4.7 (0.6) | 4.7 (0.5) |
| Important I quit smoking b | 4.2 (0.9) | 4.2 (1.0) |
| Confident I can reduce my smoking b | 3.6 (1.0) | 3.6 (1.0) |
| Confident I can quit smoking b | 3.0 (1.1) | 2.9 (1.1) |
| Frequency of urges to smoke c | 3.2 (1.2) | 3.3 (1.1) |
| Strength of urges to smoke d | 3.2 (1.1) | 3.2 (1.1) |

a IMD (https://imd-by-postcode.opendatacommunities.org/imd/2019)

b Using a 5-point Likert scale from 1 (strongly disagree) to 5 (strongly agree), reported as mean (SD)

c Using a 6-point Likert scale from 0 (not at all) to 5 (all the time), reported as mean (SD)

d Using a 6-point Likert scale from 0 (no urges) to 5 (extremely strong), reported as mean (SD)

Table 2: Primary and secondary prolonged abstinence outcomes. Values are numbers (percentages) unless stated otherwise.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcomes | Intervention (n=450) | Support as usual (n=451) | Adjusted odds ratioa (95% CI), p-value | Adjusted absolute between-group differences in risk (%)b (95% CI),p-value | Adjusted relative riskc (95% CI),p-value |
| Primary |  |  |  |  |  |
| Floating biochemically-verified 6-month prolonged abstinence between 3 and 9 months | 9 (2.0) | 4 (0.9) | 2.30(0.70 to 7.56), 0.17 | 1.12(-0.43 to 2.67), 0.16 | 2.27(0.71 to 7.29), 0.17 |
| Secondary: |  |  |  |  |  |
| Floating biochemically-verified 6-month prolonged abstinence verified between 3 and 9 months or 9 and 15 monthsd | 14 (3.1) | 10 (2.2) | 1.43 (0.62 to 3.26), 0.40 | 0.91 (-1.19 to 3.00), 0.40 | 1.41 (0.64 to 3.13), 0.40 |
| Floating biochemically-verified 12-month prolonged abstinence between 3 and 15 monthsd | 6 (1.3) | 1 (0.2) | 6.33 (0.76 to 53.10), 0.089 | 2.03 (-0.028 to 4.09), 0.053 | 6.17 (0.75 to 50.84), 0.091 |

SAU: Support as usual
Analysis adjusted for stratification variables (HSI and site)

a Odds of confirmed abstinence in Intervention group relative to SAU
b The difference in risk of confirmed abstinence subtracting SAU from Intervention group
c Relative risk of confirmed abstinence in Intervention group relative to SAU.

d Only participants with biochemically-verified abstinence at 9 months were followed up at 15 months

Table 3: Secondary smoking outcomes. Values are numbers of participants (percentages) unless stated otherwise

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcomes | Intervention (n=450) | Support as usual (n=451) | Adjusted odds ratioa (95% CI), p-value | Adjusted absolute between-group differences in risk (%)b (95% CI),p-value | Adjusted relative riskc (95% CI),p-value |
| Self-reported point prevalence abstinence: |  |  |  |  |  |
|  At 3 months d | 25 (5.5) | 13 (2.9) |  1.99 (1.00 to 3.94), 0.049 | 2.64 (0.060 to 5.23), 0.045 | 1.93 (1.00 to 3.72), 0.050 |
|  At 9 months d | 38 (8.4) | 36 (8.0) |  1.07 (0.66 to 1.72), 0.79 | 0.48(-3.10 to 4.06), 0.79 | 1.06 (0.69 to 1.64), 0.79 |
|  At 15 monthse | 16 (3.6) | 14 (3.1) | 1.15 (0.56, 2.40), 0.70 | 0.46 (-1.87 to 2.79), 0.70 | 1.15 (0.57 to 2.32), 0.70 |
| Biochemically-verified point prevalence abstinence: |  |  |  |  |  |
|  At 3 months d | 17 (3.7) | 8 (1.8) | 2.19 (0.93 to 5.14), 0.071 | 1.99 (-0.12 to 4.11), 0.064 | 2.14 (0.93 to 4.90), 0.072 |
|  At 9 months d | 25 (5.6) | 21 (4.7) | 1.21 (0.66 to 2.19), 0.54 | 0.90 (-1.97 to 3.77), 0.54 | 1.19 (0.68 to 2.10), 0.54 |
|  At 15 monthse | 11 (2.4) | 7 (1.6) |  1.61 (0.62 to 4.21), 0.33 | 0.91 (-0.91 to 2.73), 0.33 | 1.59 (0.62 to 4.04), 0.33 |
| Reduced smoking by ≥50% between baseline and 3 months | 86 (18.9) | 48 (10.5) | 1.98 (1.35 to 2.90), <0.0004 | 8.35 (3.79 to 12.91),0.0003 | 1.79 (1.29 to 2.49), 0.0005 |
| Reduced smoking by ≥50% between baseline and 9 months | 65 (14.4) | 45 (10.0) | 1.52 (1.01 to 2.29), 0.043 | 4.41 (0.17 to 8.65), 0.042 | 1.44 (1.01 to 2.05), 0.044 |
| Total daily equivalent cigarettes smoked at 3 months – n, mean (SD) | 275,21.1 (23.6) | 283, 26.8 (27.0) | **Adjusted mean difference f (95% CI), p-value:** -5.62 (-9.80 to -1.44), 0.0085 |
| Total daily equivalent cigarettes smoked at 9 months – n, mean (SD) | 244,22.6 (25.8) | 240,24.2 (23.9) | **Adjusted mean differencef (95% CI), p-value**: -0.95 (-5.37 to 3.46), 0.67 |
| Quit attempt made in first 3 monthse | 54 (11.8) | 37 (8.1) | 1.53(0.99, 2.39), 0.058 | 3.77(-0.096 to 7.64),0.056 | 1.47(0.99 to 2.18),0.058 |
| Quit attempt made between 3 months and 9 monthse | 76 (16.9) | 68 (15.1) | 1.15(0.80 to 1.64), 0.45 | 1.85(-2.92 to 6.62),0.45 | 1.12(0.83 to 1.52),0.45 |
| Vaping or LNCP use at 3 months – n/N (%) | 125/296 (42.2) | 113/288 (39.2) | 1.05 (0.74 to 1.49), 0.80 | 0.99 (-6.54 to 8.51), 0.80 | 1.02 (0.85 to 1.23), 0.80 |
| Vaping or LNCP use at 9 months– n/N (%) | 114/270 (42.2) | 96/268 (35.8) | 1.27 (0.88 to 1.83), 0.20 | 5.24(-2.67 to 13.14), 0.19 | 1.14 (0.93 to 1.40), 0.20 |

SAU: Support as usual

Analysis adjusted for stratification variables (HSI and site) and baseline measures of outcome under analysis if applicable.

a Odds of ‘success’ in Intervention relative to SAU
b The difference in risk of ‘success’ subtracting SAU from Intervention
c Relative risk of ‘success’ in Intervention group relative to SAU

d Not having smoked a puff in the past week.

e Only participants with biochemically-verified abstinence at 9 months were followed up at 15 months. Not having smoked a puff in the past week.
f 24hrs hours without smoking even a puff
g The mean difference in each outcome subtracting SAU from Intervention

Table 4: Other secondary outcomes. Values are n, means (standard deviations) unless stated otherwise

|  |  |  |  |
| --- | --- | --- | --- |
| Secondary Outcomes | Intervention  | Support as usual | Adjusted mean between-group differencea (95% CI), p-value |
| Self-reported total weekly minutes moderate-to-vigorous PA at 3 months | 308,397.7 (389.9) | 300, 319.1 (354.9) | 81.61 (28.75, 134.47),0.0025 |
| Self-reported total weekly minutes moderate-to-vigorous PA at 9 months | 273,352.9 (375.5) | 269,330.7 (360.6) | 23.70 (-33.07, 80.47),0.41 |
| Accelerometer assessed average daily minutes of moderate to vigorous physical activity at 3 monthsb | 42,95.2 (43.6) | 45,82.4 (53.6) | 13.88(-7.74, 35.50),0.21 |
| BMI at 3 months (Kg/m2) | 301,26.1 (5.8) | 288,26.7 (6.1) | -0.17(-0.50 to 0.16),0.32 |
| BMI at 9 months (Kg/m2) | 262,26.4 (6.1) | 265,26.7 (5.9) | -0.26(-0.64 to 0.11),0.17 |
| Self-reported daily average time spent sleeping over past week at 3 months | 287,7.1 (1.6) | 278,6.9 (1.7) | -0.02(-0.26 to 0.22),0.86 |
| Self-reported daily average time spent sleeping over past week at 9 months | 260,7.0 (1.8) | 247,6.7 (1.6) | 0.09(-0.19 to 0.36),0.53 |
| SF-12 (Mental component score at 3 months) | 240,44.8 (11.7) | 231,42.9 (11.6) | 1.91(0.15, 3.67),0.034 |
| SF-12 (Physical component score at 3 months) | 240,47.7 (11.1) | 231,46.7 (10.7) | 1.33 (-0.13, 2.80),0.074 |
| EQ-5D-5L utility at 3 months | 306,0.717 (0.249) | 298,0.662 (0.310) | 0.022(-0.012, 0.056),0.20 |
| EQ-5D-5L utility at 9 months | 279,0.681 (0.272) | 267,0.666 (0.295) | 0.006(-0.030, 0.043),0.73 |

SAU: Support as usual
Analysis adjusted for stratification variables (HSI and site) and baseline measures of outcome under analysis if applicable
Note; Accelerometer data was not in bouts

a The mean difference in each outcome subtracting SAU from Intervention
b Accelerometer data is from participants providing at least 4 days of data including 1 weekend day, with a daily wear-time of at least 16 hours, and adjusted for baseline self-report MVPA.
C EQ-5D-5L mapped to EQ-5D-3L utility values using the crosswalk method, mean differences estimated using linear regression26

Table 5: Mediation analysis of changes in self-report MVPA at 3 months as a mediator of intervention effects on cigarettes smoked at 3 months, and ≥50% reduction in self-reported smoking from baseline to 3 and 9 months.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Outcome  | N | A path | B path | Mediated effect | C path |
|
| coefficient (SE) | coefficient (SE) | coefficient (SE) | 95% CI | coefficient (SE) |
| Cigarettes smoked per day | 608 | **0.195 (0.064)** | 0.841 (1.102) | 0.164 (0.265) | (-0.228,0.943) | **-5.470 (2.162)** |
| Achieving ≥50% reduction in self-reported smoking at 3 months | 608 | **0.195 (0.064)** | 0.044 (0.102) | 0.009 (0.021) | (-0.032,0.053) | **0.648 (0.205)** |
| Achieving ≥50% reduction in self-reported smoking at 9 months | 608 | **0.195 (0.064)** | -0.056 (0.116) | -0.011 (0.024) | (-0.068,0.033) | 0.251 (0.232) |

Statistically significant effects at the two-sided 5% level are in bold.

Figure 1: Path model for mediating effects of changes in moderate to vigorous physical activity on smoking outcomes

Figure 2: Trial profile