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ORIGINAL ARTICLE

Exercise to Enhance Smoking Cessation: the Getting Physical on Cigarette Randomized Control Trial

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Abstract

Background Exercise has been proposed as a useful smoking cessation aid.

Purpose The purpose of the present study is to determine the effect of an exercise-aided smoking cessation intervention program, with built-in *maintenance components*, on post-intervention 14-, 26- and 56-week cessation rates.

Method Female cigarette smokers (n=413) participating in a supervised exercise and nicotine replacement therapy (NRT) smoking cessation program were randomized to one of four conditions: exercise + smoking cessation maintenance, exercise maintenance + contact control, smoking cessation maintenance + contact control or contact control. The primary outcome was continuous smoking abstinence.

Results Abstinence differences were found between the exercise and equal contact non-exercise maintenance groups at weeks 14 (57 vs 43 %), 26 (27 vs 21 %) and 56 (26 vs 23.5 %), respectively. Only the week 14 difference approached significance, p=0.08.

Conclusions An exercise-aided NRT smoking cessation program with built-in maintenance components enhances post-intervention cessation rates at week 14 but not at weeks 26 and 56.

Keywords Exercise · NRT · Maintenance · Smoking cessation

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Introduction

In 2014, an estimated 191,300 new cases of cancer and 76,600 cancer deaths were expected in Canada [1]. Lung cancer is currently the leading cause of premature death for men and women (27 % of all cancer deaths) [1]. Cigarette smoking, which causes 85 % of lung cancer cases, is the single largest preventable health problem in the world and one of humankind's most serious self-inflicted epidemics [2, 3]. Cigarette smoking is also one of the main causes of cardiovascular disease [4]. It is recognized in all Canadian health strategy documents that stopping smoking at any age is associated with clear health benefits [5].

Unfortunately, the nicotine found within cigarettes is highly addictive [6], making it difficult for many smokers who wish to quit. The relative speed at which this low-cost drug is delivered to the brain and the debilitating physiological and psychological withdrawal symptoms associated with

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refraining from smoking make it a particularly potent drug dependence addiction [7].

A significant portion of tobacco control efforts has been directed towards developing individual-based pharmacotherapy cessation interventions that target the dependency-forming properties of nicotine to promote and sustain abstinence. Despite the availability of pharmacotherapy treatments like nicotine replacement, bupropion and varenicline, the proportion of people who remain smoke free 1 year later remains modest at best (10–24 %) [8–10]. Hence, it is important to continue to look for novel ways to improve existing smoking cessation treatments.

The addition of exercise to traditional smoking cessation treatments (i.e. nicotine replacement therapy (NRT)) has the potential to improve existing cessation rates. There are numerous reasons for making this claim. For instance, meta-analyses have shown that an acute bout of exercise reduces craving following a temporary period of abstinence [11, 12]; however, the mechanisms to explain why exercise alleviates cravings are not completely understood. They include hypotheses such as changes in stress and activation [13]; positive and negative affect [11, 14]; cognitive to somatic thoughts [15]; and cortisol [16, 17], catecholamines and heart rate variability [16]. These mechanisms are different to those of NRT and, through extension, suggest that exercise can provide further craving and withdrawal relief during a quit attempt involving NRT [18, 19]. Exercise also has been shown to have a positive effect on other factors that may protect against smoking relapse, including coping with stress [19, 20], depression [21] and general fatigue and sleep disturbances [22–24]. NRT is not designed to influence these factors. Finally, targeting change in multiple health behaviours (exercise adoption and smoking cessation) has the capacity to maximize health benefits and promotion [25]. In addition, exercise has been shown to provide a protective effect against the most prevalent types of cancer including lung cancer [26].

A Cochrane review [27] of exercise-aided interventions for smoking cessation identified 20 randomized control trials (n= 5870) with at least a 6-month follow-up period. Only four [28–31] of the 20 trials showed significantly higher abstinence rates favouring the exercise-aided group at the end of treatment, while only one study showed a significant benefit of exercise at 1-year follow-up [31]. Two recent studies [32—included as an ongoing study—33] from the Cochrane review are directly relevant to the current study. The small (n=61), underpowered efficacy study by Abrantes and colleagues found clinically meaningful but non-significant differences in abstinence rates between the exercise-aided transdermal nicotine patch group and the health education-aided transdermal nicotine patch group at end of treatment (40 vs 22.6 %, odds ratio 2.28) and 12-month (26.7 vs 12.9 %, odds ratio= 2.46) follow-up, respectively. A noteworthy finding in this study was the high program adherence to the supervised exercise (mean of 9/12 sessions) as well as the telephone-delivered smoking cessation material (mean of 7/8 sessions). This was likely due to the supervised cognitive-behavioural counselling for exercise promotion, the telephone counselling for smoking cessation and the modest financial incentive components of the intervention program. Methodological limitations with this work include no indication how many smokers were off cigarettes post-exercise and post-transdermal patch treatment and no post-exercise maintenance component.

The large (n=906) and adequately powered effectiveness study by Maddison and colleagues found that a telephone-delivered exercise counselling intervention was not sufficient to improve cessation rates at 24 week follow-up over and above existing smoking cessation services that included behavioural counselling and the transdermal nicotine patch (23 vs 22 %, relative risk=0.98). The study reported that only 52 % of participants randomized to the exercise intervention group completed at least seven of the ten intervention calls and that the more calls that were successfully delivered, the lower the probability of smoking (odds ratio=0.88). The differences in exercise adherence between the two studies may be due, in part, to the financial incentive offered in the study of Abrantes et al.. This study also likely attracted participants who were more motivated and ready to exercise (i.e. required to start a supervised exercise program) than participants in the study of Maddison et al. (i.e. required to start an unsupervised exercise program). Furthermore, the exercise assessment time period was shorter in the study of Abrantes et al. (i.e. 12 weeks) than the assessment period in the study of Maddison et al. (i.e. 24 weeks). This, of course, made adherence easier in the former than latter study. These findings, taken in concert, underscore the importance of adherence to the success of exercise-aided smoking cessation programs, which has been ignored, has been unreported or, when reported, has been consistently low in previous trials [34–36].

One way to improve on adherence rates to exercise-aided smoking cessation programs that no trial has addressed thus far is to focus on the *maintenance* of both exercise and smoking abstinence. Unfortunately, access to maintenance assistance is made available to less than 10 % of smokers who follow formal cessation programs in their efforts to stop smoking [37–39]. All smoking cessation programs (including exercise-aided ones) show early success followed by rebound (relapse) effects at program termination and follow-up [10, 26]. Hence, it is imperative that these types of programs have integrated cessation and exercise maintenance components to prevent relapse in both behaviours. This important issue has been identified as a research priority in a knowledge synthesis of the exercise and smoking cessation literature [39].

In summary, there is some evidence that the addition of exercise to standard care (counselling and/or NRT) increases short-term abstinence in comparison to standard care alone, but there is little consistent evidence for long-term benefit

[26]. Two recent studies [32, 33] have produced mixed results which weaken the claim that can be made about the value of exercise as a smoking cessation aid. Our "Getting Physical on Cigarettes" trial is designed to examine whether quitters exposed to an exercise-aided NRT smoking cessation intervention program that has built-in *maintenance components* could enhance post-intervention 14-, 26- and 56-week cessation rates compared to contact controls. A secondary purpose was to determine whether treatment allocation and/or smoking status influenced adherence rates to the different program components (i.e. supervised exercise, NRT, exercise and smoking cessation maintenance).

Method

The rationale and methods for Getting Physical on Cigarettes were previously reported elsewhere [40]. In brief, participants undergoing a 14-week structured exercise program with nicotine replacement therapy (NRT) were randomized to one of four conditions: exercise maintenance + smoking cessation maintenance, exercise maintenance + contact control, smoking cessation maintenance + contact control or contact control. The trial was approved by the host institution's research ethics board and was registered with the US National Institutes of Health clinical trial registry (NCT01305447). The conduct of the trial followed the principles outlined in the Declaration of Helsinki [41] and the World Health Organization's Handbook for Good Clinical Research Practice [42].

Participants

Four hundred and thirteen female smokers wishing to quit smoking participated in this study between 2009 and 2013 (i.e. seven successive cohorts; $n \sim 60$ per cohort). Participants were recruited from local businesses, hospitals, academic institutions and organizations and through advertisements placed in newspapers, radio stations and city buses in London, Ontario. Individuals between the ages of 18 and 65 years, who smoked more than ten cigarettes/day and have done so for the past 2 years, wanted to quit smoking, engaged in two or less 30-minute bouts of moderate or vigorous intensity exercise per week over the past 6 months and were able to read and write in English were eligible to participate in the trial. Women were barred from participating if they were pregnant or were planning to become pregnant during the next year, had other substance dependency problems (e.g. alcohol), prescribed medication for physical and/or mental health reasons that would compromise compliance with the study protocol or presented with contraindications to regular exercise or using NRT.

Measures

Demographics, Smoking History and Anthropometry

Participants completed a demographic and smoking history questionnaire, which collected information such as age, level of education, household annual income and number of years smoking, at baseline. Fagerstrom Test for Cigarette Dependence was also administered [43, 44]. Weight was collected (Health-o-meter professional, Pelstar 500KL) after participants removed their shoes and heavy clothing (e.g. sweater). It was recorded to the nearest 10th of a kilogram.

Smoking Behaviour

Self-reported cigarette consumption was assessed weekly throughout the program, as well as during follow-up at weeks 14, 26 and 56. Smoking status was verified at the same intervals from expired breath carbon monoxide using the piCO+™ Smokerlyzer® (Bedfont Scientific Ltd., Kent, England). Carbon monoxide levels below 6 ppm indicated smoking abstinence [45]. These data were utilized for the primary outcome: continuous (lapse free) abstinence from quit day to end of treatment (14 weeks) and 3 (26 weeks) and 12 months (56 weeks) months after treatment. Individuals with missing data were regarded as smoking.

Leisure Exercise

Participant activity levels outside of the laboratory were monitored using self-report (Godin Leisure Time Exercise Questionnaire [LTEQ]) [46]. The LTEQ measured exercise covering the frequency of mild, moderate and strenuous exercise performed during free time for at least 15-min bouts during a typical week. For the purpose of this study, LTEQ data administered at week 26 and week 56 will be used. A total metabolic equivalent (metabolic equivalent of task (MET)) score was derived by summing the reported weekly frequency (f) of participation at each of the three intensity levels multiplied by the temporal factor and corresponding estimated METs/week value (e.g. [(mild × 3×0.25 h)+(moderate × 5× 0.25 h)+(strenuous × 9×0.25 h)]).

Program Components (Weeks 1–14)

Supervised Exercise Participants, in groups of 10–15 women, exercised in a supervised facility at the Exercise and Health Psychology Laboratory (EHPL) and used various cardiovascular machines, such as treadmills, rowing machines, stair climbers and stationary bicycles. Participants' workload (intensity and duration) progressively increased to 70–75 % of their maximum heart rate over the 14-week period as the number of exercise sessions tapered. For the

first 8 weeks of the 14-week program, participants engaged in three exercise sessions per week (45-min duration). During the remainder of the program, participants were weaned off their exercise sessions during weeks 9–14 in order to encourage exercise independence and foster the transition from laboratory-based to home-based physical activity. Specifically, participants attended two supervised sessions per week during weeks 9–11 and one supervised session per week during weeks 12–14.

Individualized exercise prescriptions were determined from maximum heart rate attained during the baseline cardiorespiratory fitness assessment and were monitored during exercise sessions using Polar heart rate monitors. Participants were expected to perform bouts of aerobic exercise at the same intensity level and duration as the lab-based exercise sessions in their home or community during the aforementioned weaning period, to achieve at least three aerobic bouts per week throughout the remainder of the 14-week program. Attendance to the 14-week supervised, aerobic exercise regimen was calculated from the number of exercise sessions attended by the participant compared to the total number of exercise sessions offered. This was converted into a percentage.

Nicotine Replacement Therapy After 4 weeks of exercising, participants were provided with transdermal NRT and followed the Nicoderm® three step, 10-week program. Accordingly, a 21-mg patch was applied once daily for weeks 4–9, followed by a 14-mg patch applied once daily for weeks 10–11 and, finally, a 7-mg patch applied once daily during weeks 12–13. To facilitate compliance with the NRT protocol, the appropriate patches were distributed to each participant on a weekly basis. Study investigators monitored the dispensing of NRT as a percentage: the number of patches supplied to participants compared to the total quantity for the aforementioned Nicoderm® protocol.

Exercise and Equal Contact Non-Exercise Maintenance Using a trained facilitator, two of the four randomized intervention arms (exercise maintenance + smoking cessation maintenance and exercise maintenance + contact control) received five 25-min weekly (weeks 8–14) cognitive behavioural therapy sessions in a group format, with the goal of teaching self-regulatory skills essential during the remainder of the program and, for long-term, independent exercise adherence [40]. For those randomized to the smoking cessation maintenance + contact control and contact control arms, messages reinforcing women's health issues (e.g. vitamin D intake, oral hygiene, sleep disorders) were communicated.

Program Components (Weeks 26 and 52)

Exercise and Equal Contact Non-Exercise Phone Maintenance Following the termination of the 14-week exercise-aided smoking cessation program, the same facilitator delivered seven 15-min biweekly (for the first month), monthly (for the next 2 months) and then bimonthly (for last 8 months) telephone counselling sessions. Participants randomized to the exercise maintenance + smoking cessation maintenance and exercise maintenance + contact control arms received telephone counselling to maintain exercise behaviour. For those randomized to the smoking cessation maintenance + contact control and contact control arms, messages reinforcing the Forever Free booklets and/or women's health issues (e.g. vitamin D intake, oral hygiene, sleep disorders) were once again communicated. The content of the telephone maintenance program has been previously described in greater detail [40]. Participation in the Exercise Maintenance Program was calculated from the number of counselling sessions received compared to total number of counselling sessions and expressed as a mean percent. Call duration and number of call attempts to the telephone maintenance program for all participants were tracked.

Smoking Cessation Maintenance (Forever Free Booklets) After the conclusion of the 14-week exercise-aided NRT smoking cessation program, participants randomized to the exercise maintenance + smoking cessation maintenance and smoking cessation maintenance + contact control arms received a set of Brandon's "Forever Free" booklets [39, 47, 49]. The content of these booklets spoke to the behaviour of smoking cessation and relapse prevention. In specific, evidence-based information on topics such as urges, weight gain, stress and lifestyle balance was provided. For participants who were unable to attend their week 14 assessment, the set of eight booklets were mailed to their home address.

Procedure

Prior to study enrolment, eligible individuals provided written informed consent and medical clearance. Participants completed baseline testing, which involved the confirmation of smoking status and the completion of questionnaires. Data for other secondary outcome measures were collected; however, they are not reported here. Assessments were completed at the EHPL (ehpl.uwo.ca) in London, Ontario. The supervised exercise and NRT regimen occurred during weeks 1–14 and 4–13, respectively. Supervised exercise was offered prior to the quit date at week 4 because exercise and smoking are not compatible behaviours, thus providing smokers the opportunity to replace a harmful behaviour with one that is beneficial. Exercise can be seen as a gateway to smoking cessation, which is supported by previous

research [31–33, 48–50] which did not instruct participants to decrease cigarette consumption before their quit date (approximately 3–4 weeks away). The decision to start the NRT program at week 4 was based on two considerations. First, week 4 was the targeted quit week where participants would likely need additional support for their quit attempt. Second, the NRT program was 10 weeks and the supervised exercise program was 14 weeks. Hence, both programs would terminate together.

Using a computer-generated sequence, participants were randomized at week 8 of the program. The project manager for trial used numbered containers to implement the random allocation sequence, and the sequence was concealed until interventions were assigned. Irrespective of treatment allocation, all participants completed follow-up testing at weeks 14, 26 and 56. These assessments mirrored baseline testing, whereby self-reported and objective verification of smoking status were provided. Research assistants conducted assessments according to standard procedures and were not blinded to treatment allocation. A flow diagram illustrates how participants moved through the trial (see Fig. 1).

Sample Size

The trial was designed to randomize 420 participants, with complete data for an estimated 300 participants (projected dropout, 120 participants) at the end of 12-month follow-up (approximately 75 in each of the four conditions). This was projected to provide power of 80 % ($p<0.01$) and to detect a 19 % difference between treatment conditions (e.g. 35 %) and contact control (e.g. 16 %) on the primary variable of interest, continuous smoking abstinence [51, 52]. Our estimated treatment effect is larger than what has been shown in other exercise-aided smoking cessation trials [31, 33]. This is because no previous trial has implemented both *cessation and exercise maintenance components* to specifically enhance post-treatment cessation rates. A total of 413 participants were enrolled due to recruitment challenges encountered.

Statistical Analyses

One-way analysis of variances (ANOVAs) and chi-square were used to test for group equivalency on baseline socio-demographic and smoking history variables amongst the four treatment conditions. For the primary outcome, chi-squared analyses were used to compare continuous abstinence between treatment conditions at weeks 14, 26 and 56. As a sensitivity analysis, the primary outcome was assessed (chi-squared) only among those participants with data at each time point across the study period. Treatment condition by smoking status factorial ANOVA was used to test for differences in adherence to structured exercise, NRT and telephone maintenance. Statistical significance was assumed at $p=0.05$, and results were based on two-tailed statistical tests. Data were analyzed using SPSS for Windows version 22 (IBM, USA).

Results

Missing Data

There were no significant differences in the demographic variables of weight, education, household annual income and METs as well as baseline smoking CO levels for those that provided complete vs missing primary end point cessation data (all p values >0.05). Those that did provide complete end point cessation data were older (45.24 vs. 39.87 years), more likely to be married (54.5 vs 45.5 %), smoked fewer cigarettes per day at baseline (16.37 vs. 17.2), smoked for more years (24.5 vs. 20.2) and had lower Fagerstrom Test for Cigarette Dependence scores (5.2 vs 5.5) than counterparts that had missing data (all p values <0.05). Furthermore, there were no significant missing end point cessation data differences between treatment groups (all p values >0.05). Taken together, all missing data was not considered completely random.

Treatment Group Equivalency

Descriptive statistics for socio-demographic factors, smoking behaviour and history and adherence are presented in Table 1, with no observed differences between treatment groups. One adverse event (participant from the smoking cessation maintenance + contact control group) was reported but was unrelated to the intervention.

Smoking Cessation (Primary Outcome)

At week 14, 40.30 % (167 of 413) of participants demonstrated continuous smoking abstinence. Differences in smoking status between the exercise maintenance groups (56.90 %, 95 of 167 smoke free) and contact control groups (43.10 %, 72 of 167 smoke free) approached significance (χ^2 [1, n=409]=2.36, p=0.08).

Continuous smoking abstinence at week 26 was 21.50 % (89 of 413) of all participants. Exercise maintenance + smoking cessation maintenance (30.30 %, 27 of 89), exercise maintenance + contact control (25.80 %, 23 of 89), smoking cessation maintenance + contact control (23.60 %, 21 of 89) and contact control (20.20 %, 18 of 89) groups did not significantly differ (χ^2 [3, n=409]=1.14, p=0.77) in the proportion of abstinent participants.

At week 56, 14.00 % (58 of 413) of participants achieved continuous smoking abstinence. Exercise maintenance + smoking cessation maintenance (32.80 %, 19 of 58), exercise maintenance + contact control (19.00 %, 11 of 58), smoking

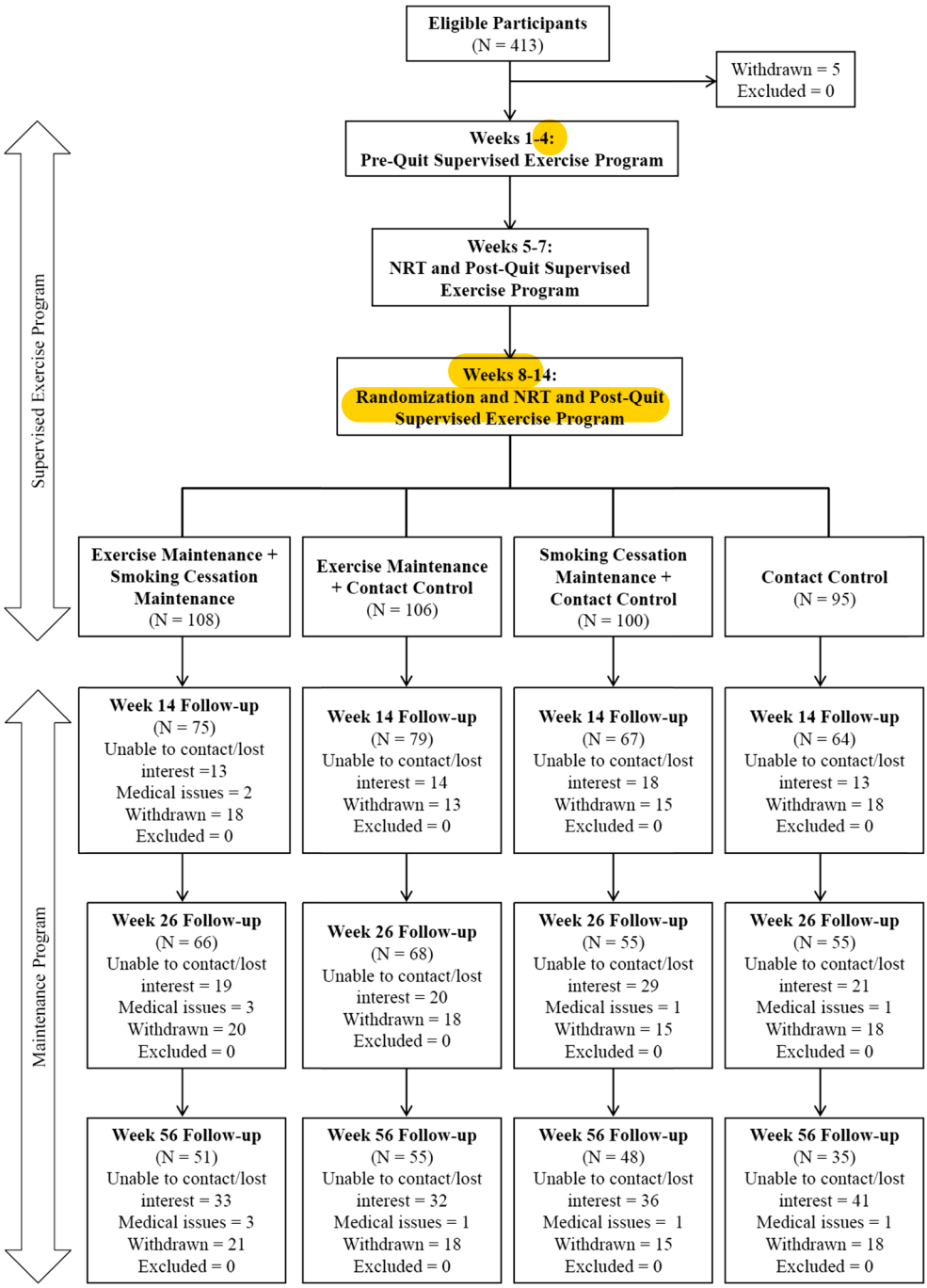

Fig. 1 Flow diagram of participants throughout the trial

cessation maintenance + contact control (27.60 %, 16 of 58) and contact control (20.70 %, 12 of 58) groups did not significantly differ (χ^2 [3, n=409]=2.75, p=0.43) in the proportion of abstinent participants.

Sensitivity Analyses

As a sensitivity analysis, smoking cessation rates across the study period were assessed only for participants with complete data at each time point. For continuous abstinence at week 14, 58.80 % (160 of 272) of participants were smoke free. No significant differences (χ^2 [1, n=272]=0.53, p=0.27) were found between the exercise maintenance (56.25 %, 90 of 160) and contact control (43.75 %, 70 of 160) groups.

For participants who provided data at week 26, 38.80 % (87 of 224) achieved continuous abstinence. The four groups did not significantly differ (χ^2 [3, n=224]=0.64, p=0.89) in smoking cessation rates: exercise maintenance + smoking cessation maintenance (28.7 %, 25 of 87), exercise maintenance + contact control (26.40 %, 23 of 87), smoking cessation

Table 1 Baseline characteristics for participants and percent adherence to program components

Variable	Exercise + smoking cessation maintenance	Exercise maintenance + contact control	Smoking cessation maintenance + contact control	Contact control
N	108	106	100	95
Age (years)	41.96 (12.70)	43.47 (14.02)	43.45 (12.22)	40.36 (11.92)
Weight (kg)	74.96 (17.21)	73.70 (16.85)	72.53 (15.50)	72.45 (15.53)
Marital status (*N*, %)				
Single	28 (25.9 %)	38 (36.2 %)	28 (28.3 %)	33 (35.9 %)
Married	32 (29.6 %)	35 (33.3 %)	32 (32.3 %)	19 (20.7 %)
Divorced/separated	32 (29.6 %)	13 (12.4 %)	26 (26.3 %)	21 (22.8 %)
Other	16 (14.9 %)	20 (18.1 %)	14 (13.1 %)	22 (20.6)
	13.87 (1.98)	14.00 (2.06)	13.85 (2.25)	13.69 (2.45)
Household annual income (*N*, %)				
<$50,000	54 (50.8 %)	50 (48.1 %)	53 (54.1 %)	52 (57.2 %)
$50,000–$75,000	23 (21.7 %)	18 (17.3 %)	16 (16.3 %)	14 (15.4 %)
>$75,000	20 (18.9 %)	27 (25.9 %)	22 (22.5 %)	17 (18.7 %)
Years smoking regularly	22.78 (12.30)	21.35 (12.60)	24.40 (12.72)	20.28 (11.82)
Cigarettes per day	17.04 (6.79)	16.71 (6.96)	16.88 (5.16)	16.41 (6.78)
Carbon monoxide (ppm)	19.62 (11.71)	20.37 (11.25)	20.95 (12.05)	21.44 (11.65)
Fagerstrom test for cigarette dependence, score	5.31 (2.15)	5.42 (1.68)	5.50 (1.98)	5.23 (2.22)
METS	5.76 (7.95)	5.27 (5.05)	5.70 (5.29)	6.38 (9.26)
Percent adherence				
Week 1–8 exercise	68.13 (28.80)	70.13 (28.90)	74.21 (27.80)	73.77 (27.79)
Week 9–11 exercise	54.94 (40.78)	55.82 (39.98)	55.33 (38.63)	53.68 (39.66)
Week 12–14 exercise	50.93 (47.46)	53.15 (46.41)	49.33 (43.55)	45.26 (44.01)
NRT	68.61 (35.85)	69.34 (34.46)	70.10 (34.66)	70.00 (33.55)
Telephone maintenance	37.96 (32.92)	38.54 (31.56)	43.14 (33.85)	36.09 (30.26)

Mean (SD) is reported unless otherwise stated

ppm parts per million, *NRT* nicotine replacement therapy

maintenance + contact control (24.10 %, 21 of 87) and contact control (20.70 %, 18 of 87).

For complete data at week 56, 29.90 % (58 of 194) of participants achieved continuous abstinence. Exercise maintenance + smoking cessation maintenance (32.80 %, 19 of 58), exercise maintenance + contact control (19.00 %, 11 of 58), smoking cessation maintenance + contact control (27.60 %, 16 of 58) and contact control (20.70 %, 12 of 58) groups did not significantly differ (χ^2 [3, n=194]=4.11, p=0.25) in the proportion of abstinent participants.

Adherence (Secondary Outcomes)

Program Components (Weeks 1–14)

Supervised Exercise Overall, participants completed 70.75 % (SD=29.08), 54.44 % (SD=39.83) and 49.31 % (SD=45.42) of their supervised exercise sessions during weeks 1–8, 9–11 and 12–14, respectively. Non-significant differences in percent adherence to the exercise program during weeks 1–8 (F (1, 408)=3.03, p=0.08), 9–11 (F (1, 408)=0.046, p=0.83) and 12–14 (F (1, 408)=1.08, p=0.30) were found between those randomized to the exercise maintenance groups versus the contact control groups. On the other hand, significant differences in percent adherence to the supervised exercise program during weeks 1–8 (F (1, 412)=70.07, p<0.001), 9–11 (F (1, 412)=136.45, p=0.00) and 12–14 (F (1, 412)=121.89, p<0.001) were exhibited across those classified as smoking and non-smoking, based on continuous smoking abstinence. The interaction effect of randomization and smoking status on exercise program adherence was non-significant (F (1, 409)=0.00, p=0.98).

Nicotine Replacement Therapy Participants completed 68.81 % (SD=35.04) of their NRT protocol. Significant differences in percent adherence to the 10-week NRT program did not surface (F (1, 409)=1.08, p=0.30) between those randomized to the exercise maintenance groups (M=70.86, SE=2.12) versus the contact control groups (M=74.10, SE=2.28). Similarly, significant differences (F (1, 409)=131.042, p<0.001) in percent adherence to the NRT protocol were exhibited across those classified as smoking (M=56.33, SE=

1.98) and non-smoking (M=88.63, SE=2.24), based on continuous smoking abstinence. The interaction effect of randomization and smoking status on NRT was non-significant (F (1, 409)=0.19, p=0.67).

Exercise Maintenance The mean attendance to the maintenance component (exercise maintenance and equal contact women's health issues), which occurred during weeks 8 to 14 of the intervention, was 53.81 % (SD=37.88). Differences in adherence did not reach statistical significance (F (1, 409)=1.00, p=0.32) between those randomized to the exercise maintenance groups (M=56.35, SE=2.23) versus the contact control groups (M=59.63, SE=2.40). Participation in the aforementioned intervention maintenance programs was significantly different (F (1, 409)=144.87, p<0.001) between participants classified as smokers (M=38.27, SE=2.08) and non-smokers (M=77.70, SE=2.53), according to continuous smoking abstinence. The interaction effect between randomization and continuous abstinence was not significant (F (1, 409)=0.24, p=0.63).

Program Components (Weeks 26 and 52)

Exercise Phone Maintenance The mean call duration and number of call attempts to the telephone maintenance component between weeks 14 to 56 for all participants were 9.56 min (SD=3.75) and 1.76 (SD=0.52), respectively. Descriptive statistics for mean percent adherence to the telephone maintenance component between treatment groups can be found in Table 2. At week 26 (F (3, 409)=1.26, p=0.29) and 52 (F (3, 409)=0.94, p=0.42), treatment group differences in percent adherence were non-significant.

Descriptive statistics for mean percent adherence to the telephone maintenance component between smokers and non-smokers according to continuous abstinence can be found in Table 3. Percent adherence to the telephone maintenance program significantly differed between participants classified as smokers and non-smokers at week 26 (F (1, 409)=68.73, p<0.001) and also at week 56 (F (1, 409)=56.79, p<0.001). The interaction effect of randomization and smoking status on adherence to the telephone maintenance program was non-significant at week 26 (F (3, 409)=0.38, p=0.77) and at week 56 (F (3, 409)=0.24, p=0.87).

Post-Intervention Leisure Exercise

Descriptive statistics for total METS between exercise maintenance and contact control groups can be found in Table 4. A group by time repeated measures ANOVA demonstrated that total METS significantly increased from baseline, week 26 and week 56 (F [2, 59]=11.08, p< 0.001, η^2=0.27), but the interaction effect was non-significant (F [2, 59]=0.34, p= 0.71, η^2=0.01).

Descriptive statistics for total METS between those classified as smoking versus non-smoking based on continuous smoking can be found in Table 5. For week 26, non-significant (F (1, 147)=0.32, p=0.57) MET differences were found between participants classified as smoking versus non-smoking. The interaction effect of randomization and smoking status on week 26 leisure exercise MET was also non-significant (F (1, 147)=0.36, p=0.55). For week 56, non-significant MET differences (F (1, 147)=0.38, p=0.54) were found between participants classified as smoking vs. non-smoking. The interaction effect of randomization and smoking status on week 56 leisure exercise was also non-significant (F (1, 147)=0.41, p=0.52).

Discussion

The purpose of this trial was to determine whether an exercise-aided NRT smoking cessation intervention program that has built-in maintenance components could enhance post-

Table 2 Descriptive statistics for adherence to the exercise phone maintenance component of the program by treatment group allocation

Treatment Groups	Ex + smok cess main		Ex + contact control		Smok cess main + contact control		Contact control	
	M	SE	*M*	SE	*M*	SE	*M*	SE
Percent adherence Exercise	64.43	2.93	66.09	2.93	68.85	2.94	69.30	2.94
Phone maintenance (Week 26)	47.13	3.95	49.06	3.66	56.18	3.86	50.22	3.63
Percent adherence Exercise	64.43	2.93	66.09	2.93	68.85	2.94	69.30	2.94
Phone maintenance (Week 52)	45.98	3.32	44.32	3.76	42.61	3.84	38.82	3.87

Ex Exercise, *Ex + smok cess main* exercise + smoking cessation maintenance

Table 3 Descriptive statistics for adherence to the exercise phone maintenance component of the program by smoking status

Variable	Smoker		Non-smoker	
	M	SE	*M*	SE
Percent adherence				
Exercise	61.56	1.75	83.07	2.00
Phone maintenance				
(Week 26)	47.07	2.19	59.79	3.62
Percent adherence				
Exercise	61.16	1.76	83.44	1.86
Phone maintenance				
(Week 52)	37.61	2.10	55.94	3.43

intervention 14-, 26- and 56-week cessation rates. Those in the exercise maintenance groups had a 14 % higher continuous smoking cessation rate than those in the equal contact non-exercise maintenance groups at 14 weeks post-intervention (57.1 vs 42.9 %). These data approached statistical significance and suggest that adding an exercise maintenance component at week 8 of a structured supervised exercise-aided NRT cessation program produced some early benefits. Unfortunately, the underlying mechanisms that might explain these cessation differences (e.g. improved mood) were not explored.

Significant continuous abstinence differences were, however, not found across treatment conditions at either 26 or 56 weeks. A close examination of continuous abstinence shows that participants in the exercise maintenance + smoking cessation arm had the highest cessation rates at 26 (30 %) and 56 weeks (33 %), respectively. Furthermore, continuous abstinence at 26 and 56 weeks shows that both exercise maintenance arms had higher cessation rates (27 and 26 %, respectively) than the equal contact non-exercise maintenance arms (21 and 23.5 %, respectively). Although the 6 and 2.5 % differences at 26 and 56 weeks were not statistically significant, it may be nonetheless clinically relevant [53].

The trial did not have sufficient power to detect an absolute difference of less than 19 %. Using the 14 and 6 % differences

Table 4 Descriptive statistics for post-intervention leisure exercise by treatment group allocation

	Exercise maintenance groups		Contact control groups	
	M	SD	*M*	SD
MET				
Baseline	5.51	6.64	6.04	7.52
Week 26	8.34	6.68	7.59	6.19
Week 52	8.65	6.78	9.78	18.13

Table 5 Descriptive statistics for post-intervention leisure exercise by smoking status

Variable	Smoker		Non-smoker	
	M	SE	*M*	SE
MET				
Week 26	7.73	0.66	8.37	0.91
Week 52	8.80	1.27	10.24	1.94

MET metabolic equivalent of task

found between exercise maintenance vs equal contact non-exercise maintenance arms, a sample size of 200 (instead of 167) and 790 (instead of 89) in each arm would be needed to detect with adequate power (0.80) a statistically significant difference in cessation rates at 14 and 26 weeks, respectively.

Despite these potential clinically meaningful differences, the 26- and 52-week follow-up end point findings suggest that a telephone-delivered exercise counselling maintenance may not be sufficient to substantially improve long-term cessation rates over and above smoking cessation maintenance (Forever Free booklets) or contact control. This, of course, raises the question why? Irrespective of treatment allocation, adherence to the structure supervised exercise-aided NRT smoking cessation component (i.e. 66 % for exercise and 68 % for NRT) as well as the exercise maintenance component delivered during weeks 8–14 of the intervention (i.e. 54 %) was substantially higher than adherence to the post-intervention telephone maintenance component (i.e. 38 %) of the cessation program. Hence, participants were more motivated to complete the face-to-face intervention and maintenance component than the telephone maintenance component offered post-intervention.

Smoking status, and not treatment allocation or the interaction, was found to be consistently related to adherence across the entire trial. That is, abstainers had higher adherence rates than their smoking counterparts. This suggests that staying involved with exercise, NRT and maintenance components of this program is associated with improved cessation rates. It also suggests that those who relapsed (particularly early) decided not continue to receive treatment. Identical contact time was provided to all treatment arms by offering health education material. This allowed us to distinguish the specific effect of exercise and smoking cessation maintenance from the non-specific impact of receiving more maintenance. Hence, irrespective of treatment arm, those who received more maintenance were more likely to remain smoke free.

These findings raise another question: what can be done in the future to improve not only the adherence to maintenance but also the effectiveness of the content of maintenance, particularly post-intervention maintenance? For instance, when we were able to connect with participants via phone, the review calls could not be timed with when a participant required the most

help. In addition, a number of participants in the exercise condition wanted more from the exercise facilitator than advice on "how to keep exercising" or a reminder to "refer to your smoking relapse booklet". These factors, taken in concert, suggest that more effective, individualized, accessible, yet cost-sustainable follow-up maintenance options should be explored. Systematic reviews support the efficacy of internet and mobile interventions for short-term improvements in smoking cessation and exercise; however, results in support of their effectiveness on long-term abstinence are equivocal [54, 55] and on long-term exercise participation are unknown [56, 57]. This avenue of research warrants attention.

There were no treatment group differences in post-leisure exercise at either 26 or 56 weeks. Post-leisure exercise also could not be discriminated by smoking status or the interaction of treatment group by smoking status. There was, however, a significant time effect indicating that all participants increased their post-leisure exercise from baseline, and this increase approached the bottom range of MET units per week (14–23) [58] and lower end of energy expenditure (1000 kcal per week) [59] for achieving some health benefit. Overall, these findings are consistent with other similar trials that have yet to demonstrate an effective approach to increasing post-intervention exercise in a way that may impact smoking cessation [27]. Exercise is beneficial for a wide range of other health risks and outcomes; hence, it is important to encourage insufficiently active people who smoke to be more active. Future work may want to examine not only cessation rates in exercise-aided smoking cessation programs, but also cigarette consumption. If exercise leads to reductions in cigarettes smoked, this in turn may ultimately lead to successful cessation [60]. Exercise may have positive effects on delaying or reducing tobacco-related morbidity and mortality in both abstinent and non-abstinent smokers [26]. Examples of harm reduction benefits include a lower incidence of lung carcinoma and improved cardiovascular disease biomarker profile [61, 62].

Overall, our continuous abstinence rates (40.3 % at 14 weeks, 21.5 % at week 26 and 14 % at week 52) suggest that our exercise-aided smoking cessation program with built-in maintenance components was either superior [20, 33] or in line [31, 32] with other similar programs. Furthermore, the 14- and 26-week abstinence rates are consistent with those reported using varenicline [63, 64].

Strengths of this trial include its large sample (largest of its kind to offer a structured supervised exercise-aided smoking cessation program with built-in smoking and exercise maintenance components), the peer-reviewed design, the objective measure of exercise during treatment and the reliable and valid measure of smoking behaviour. Limitations of this trial were the relatively high loss to end of intervention and post-intervention assessments of smoking status, which is not uncommon in cessation trials [34, 65, 66]. Specifically, 14-, 26- and 56-week smoking status end point data were obtained for 65.8, 54.2 and 46.9 % of participants, respectively. Using an intention-to-treat approach, participants who did not provide end point data were treated as smokers. This, of course, can attenuate treatment effects. The sensitivity analysis using only observed data, however, does not support this notion. Continuous smoking abstinence rates for the sensitivity analysis were comparable to rates for the intent-to-treat analysis. It was also not possible to blind participants to their allocated treatment arm. Uptake of the structure exercise, NRT and exercise maintenance component of the 14-week cessation program was adequate but not uptake of post-intervention exercise phone maintenance component of the program. This negatively affected the success of this program component, given the effect that post-intervention exercise phone maintenance adherence had on smoking quit rates. There was also no formal manipulation check for the smoking cessation maintenance Forever Free booklets. Hence, we cannot say for certain that those who were offered this treatment actually received it. Our findings can only be generalized to female smokers. Finally, post-intervention exercise was assessed subjectively (i.e. self-report) rather than objectively (i.e. accelerometer) and may not have been sensitive enough to distinguish between exercise and non-exercise maintenance treatment groups.

Conclusions

Smokers attempting to quit that are exposed to an exercise-aided NRT smoking cessation intervention program that has built-in maintenance components enhance their post-intervention cessation rates at week 14 but not at weeks 26 and 56.

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Compliance with Ethical Standards

Contributors HP conceived the study. SD, LF, GF, RM and HP contributed to the final design of the study. SD, LF and SB executed the study. SD and HP ran the statistical analysis of the study. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. SD and HP prepared the first draft of the manuscript that was jointly interpreted and edited by the other authors. All authors contributed to and approved the final version of the manuscript.

Authors' Statement of Conflict of Interest and Adherence to Ethical Standards All the listed authors declare that they have no conflict of interest. All procedures, including the informed consent process, were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. The funders

(Canadian Cancer Society) played no role in the design, conduct or analysis of the study nor in the interpretation and reporting of the study findings. The researchers were independent of the funders.

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