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Citation
Mansour, M. B. L., Crone, M. R., Weert, H. C. van, Chavannes, N. H., & Asselt, K. M. van. (2024). A stop-smoking strategy after cervical cancer screening: results of a cluster-randomized controlled trial in Dutch general practice. *Nicotine & Tobacco Research*. doi:10.1093/ntr/ntae285

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Note: To cite this publication please use the final published version (if applicable).

Nicotine and Tobacco Research, 2024, **XX**, 1–10
https://doi.org/10.1093/ntr/ntae285
Advance access publication 30 November 2024
Original Investigation

A Stop-Smoking Strategy After Cervical Cancer Screening: Results of a Cluster-Randomized Controlled Trial in Dutch General Practice

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Abstract

Introduction: This study aimed to assess whether brief stop-smoking advice given to women who smoke and visit their general practice for cervical cancer screening improves smoking cessation outcomes.

Aims and Methods: This two-arm cluster-randomized controlled trial was conducted in 75 Dutch general practices. Participants in the intervention group received brief stop-smoking advice based on the Ask-Advise-Connect method, delivered by a practice assistant. Patient-reported outcomes were measured at 6 months: undertaking a serious quit attempt of at least 24 hours during follow-up (primary outcome), 7-day point prevalence abstinence at 6 months, reduction in number of cigarettes smoked, increase in motivation to quit smoking, exposure to advice or support, and other psychological and behavioral measurements.

Results: There was no significant difference in undertaking a serious quit attempt between the intervention (39.8% of $n = 266$) and control group (36.0% of $n = 214$), odds ratio 1.18 (95% confidence intervals: 0.80–1.72, $p = .41$). Neither did the point prevalence abstinence significantly differ between groups: 21.1% versus 16.3%, odds ratio 1.38 (95% confidence interval: 0.83–2.29, $p = .21$). Although nonsignificant, the direction of effects for the aforementioned outcomes was in favor of the intervention group. The reduction in the number of cigarettes smoked and increase in motivation to quit did not differ between groups. The uptake of cessation counseling was higher in the intervention (14.7%) than in the control group (2.8%).

Conclusions: A brief stop-smoking strategy after the smear test for cervical screening might encourage women who smoke to attempt quitting and seek cessation counseling, but a significant effect could not be demonstrated in this trial.

Implications: The results of this cluster-randomized trial suggest that brief advice to stop-smoking delivered by a practice assistant after routine cervical screening in general practice might encourage women who smoke to attempt quitting, but a significant effect could not be proven. Also, women who receive advice show a higher uptake of professional cessation counseling compared to their controls. Providing brief advice after the cervical smear might therefore be a useful opportunistic approach to stimulate cessation in women who smoke.

Introduction

Women are at an increased risk of developing tobacco-related diseases compared to men.[1,2] Evidence shows that the incidence of tobacco-related cancer among women in Europe is on the rise, in contrast to the declining incidence observed in men.[3] Approximately 10%–19% of all cancer diagnoses in women are attributable to smoking,[4–6] and tobacco consumption is responsible for two-thirds of deaths among women who smoke aged 50–70 years.[7]

To prevent early death and morbidity associated with smoking, cessation is crucial,[7,8] ideally at an age when the prevalence of tobacco-related diseases remains low.[8] In clinical settings, advice and support for stopping smoking can be provided.[9,10] Despite clear guidelines,[11] these opportunities are often underutilized,[12,13] particularly among people who smoke who do not yet exhibit symptoms related to smoking.[14–16] In reducing the burden of preventable cancer cases, both prevention through smoking cessation and cancer screening programs are employed.

Cancer screening programs can serve as a teachable moment for behavioral change.[17] Cervical cancer screening presents an opportunity to routinely provide women who smoke with stop-smoking advice and support, thereby creating a link between the reason for their visit (cancer prevention) and their behavior (smoking). Smoking is a risk factor for persistent

Received: April 25, 2024. Revised: September 28, 2024. Accepted: November 26 2024.
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high-risk human papillomavirus infection of the cervix, as well as for carcinoma in situ and cervical cancer.[18–21] In Europe, the population attributable fraction of smoking for cervical cancer was estimated to be 6.3%, with the population attributable fraction in Western and Northern Europe being 11.9% and 7%, respectively.[5]

In most cervical cancer screening programs, women aged 25–60 are invited every 1–5 years. In the Netherlands, women aged 30–60 years are invited for cervical cancer screening every 5 years. Among women in this age category, the smoking prevalence was reported to be 19.3%–21.3% in 2022.[22] In the Netherlands, cervical cancer screening smears are taken in general practice, where the practice assistant (PA) performs the procedure. Since 2017, women have had the option to select a self-test screening test. In 2022, 46% of eligible women underwent cervical screening, with 258 153 (35.8%) having their smears taken in their general practice.[23] We hypothesize that smoking cessation could be encouraged in this age group through an intervention linked to cervical cancer screening. For this purpose, the Ask-Advise-Connect (AAC) method is deemed appropriate because it proactively connects motivated people who smoke to professional smoking cessation support.[24,25]

In this cluster-randomized trial, we aimed to study the effect of a brief stop-smoking strategy delivered by PAs after cervical cancer screening in Dutch general practices on smoking cessation outcomes.

Methods

Study Design

The SUCCESS (smoking cessation strategy in the national cervical cancer screening program) study was a pragmatic, two-arm cluster-randomized controlled trial conducted in Dutch general practices between September 2018 and April 2022. The procedures are described in detail in the published study protocol.[26] The Dutch Ministry of Health, Welfare and Sport approved the trial following an advisory report from the Health Council (Nr. 2018/17)[27] and granted a licence to conduct the study under the Population Screening Act. The trial was registered with the Dutch Trial Register under number NL5052 (NTR7451) before its commencement (www.onderzoekmetmensen.nl/nl/trial/23461). A process evaluation (PE) was conducted in parallel with this effect study[26]; its results will be published elsewhere.

Study Participants and Recruitment

General practices, serving as the clusters, were recruited consecutively by letter and/or phone. All women attending cervical cancer screening at a participating practice were invited to participate in a lifestyle questionnaire study by the PA conducting the smear test. Women were invited before their smoking status was assessed to minimize selection bias.[26] They received both verbal and written information about the purpose of the study (Appendix 1: patient information and consent form). The number of eligible participants could not be assessed, as invitations for the cervical smear are sent by the national screening organization. Due to time constraints practices could not register how many women visited the practices for cervical screening or were invited for study participation. At study commencement, practices are reported to perform around 50–300 smears per year, depending on practice size. During the study period, smoking prevalence was around 20% among Dutch women aged 30–60 years.[26,28] Written consent was obtained prior to participation. The participants could withdraw from the study at any time. Details in the informed consent regarding the stop-smoking strategy were omitted to minimize selection bias (ie, inclusion regardless of motivation to stop-smoking or heaviness of smoking) and to not influence genuine participant behavior.[26]

Randomization and Blinding

Randomization occurred at the general practice level, with practices allocated 1:1 to either the "SUCCESS study stop-smoking strategy" or the usual care condition, using the randomization algorithm in Castor EDC. Cluster randomization was used to minimize contamination by the PA who delivered the strategy. Individual female participants were assigned the condition of the practice they visited. It was not possible to blind the recruiter, as the PAs were responsible for recruiting participants. The researchers remained blinded to the treatment allocation of individual study participants until the completion of the data analysis and to the treatment allocation of practices during the data analysis. The researchers did not participate in the follow-up appointments. An independent research assistant anonymized the dataset by removing identifying information and group labels.

Procedures

The stop-smoking strategy was administered to all women attending intervention practices for cervical screening immediately after their smear test. Based on the AAC method,[24,25] the strategy comprised the following steps: (1) ask about smoking status, (2) advise: provide brief stop-smoking advice, and (3) connect: actively offer an appointment for stop-smoking support within the practice. The survey was not used to assess smoking status, PAs were instructed to ask all women about their smoking status after the smear regardless of participation in the study.[26] During the Advise step, the PA created a teachable moment by linking the visit's purpose (namely, early detection of cancer) with the individual's health behavior (namely, smoking).[17,29] Example sentences were available for PAs (Appendix 2), as well as a leaflet for women who smoke (Appendix 3). PAs from intervention practices received training from a certified trainer to deliver the stop-smoking strategy in a one-time session before the study commenced in their practice, focusing on interviewing techniques.[26] Smoking cessation counseling itself was not part of the strategy, connected participants received the counseling available within their general practice.[26]

In control practices, the strategy was not delivered. These participants received care as usual, they only had their cervical smear taken, without the assessment of smoking status or a conversation about smoking. In both study arms, data including demographics, smoking status, and several lifestyle factors were collected through a baseline questionnaire.

At the 2-week follow-up, the participants from the intervention group received a questionnaire related to PE. At the 6-month follow-up, the participants from both study arms were sent a questionnaire via secure email or post to collect outcome measurements for both the effect study and the PE.

Measurements

At baseline, demographic variables and baseline characteristics were collected, including smoking status, age, educational level, and lifestyle behavior. The participants self-reported

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whether they considered themselves to be smoking daily or non-daily, detailing the average number of cigarettes smoked per day.[26]

The primary outcome was defined as a serious quit attempt lasting at least 24 hours during the 6-month follow-up period (serious quit attempt).[26] Secondary outcomes included 7-day point prevalence abstinence (PPA),[26] an increase in motivation to quit smoking (MTSS),[26] a reduction in the number of cigarettes smoked per day.[26]

Psychological and behavioral measurements comprised: (1) smoking-related measurements: 6 months continuous abstinence (continuous abstinence), 24-hour PPA (ie, not having smoked in the 24 hours prior to completion of the survey at 6 months), Heaviness of Smoking Index, relapses since the quit attempt and the smoking status of the partner[26]; (2) exposure to the stop-smoking strategy after the smear (to assess if participants received the strategy as intended, consisting of the AAC steps), exposure to stop-smoking advice delivered by health care professionals during another health care visit during follow-up (after the intervention or appointment for the smear up to 6 months, not part of the strategy), and the use of stop-smoking support or counseling during follow-up[26]; (3) constructs related to smoking: self-efficacy, smoker and nonsmoker identity, perceived risk, and health perception[26]; (4) general measurements: children, comorbidity, and marital status.[26]

Statistical Analysis

Power Analysis

Among women who smoke aged 30–60 years, 34% made a serious quit attempt in 2016.[28] To assess whether the "SUCCESS study stop-smoking strategy" led to an absolute increase in the performance of a quit attempt over a 6-month follow-up period from 34% in those receiving usual care (control group) to 44% in the intervention group, with 80% power at a one-sided significance level of 0.05, a sample size of 330 participants per group was necessary. The sample size calculation was adjusted for the design effect of the clustered trials.[30,31] We assumed an intracluster correlation coefficient (ICC) of 0.0130 based on previous smoking cessation interventions in general practice.[26] Considering the prevalence of smoking among women aged 30–60 years (21.6% in 2016)[28] and the number of visits for cervical screening, the aim was to recruit 10 women who smoke per cluster, resulting in 33 clusters per study arm.

Descriptives and Intention-to-Treat Analyses

For baseline variables, means with SDs and counts with percentages were calculated using IBM SPSS Statistics 28.

Primary analyses of the primary and secondary outcomes were conducted on an intention-to-treat basis. For the main analysis, we employed penalized imputation (PI): individuals with missing outcomes were conservatively assumed to have not made a quit attempt (missing primary outcome) or to have not been abstinent for the past 7 days (missing 7-day PPA).[32] Missing values for MTSS or number of cigarettes per day at follow-up were imputed following the last observation carried forward principle. For both the primary and secondary outcomes, mixed-effects logistic regression models were used to assess the stop-smoking strategy's effectiveness, incorporating a fixed effect for the strategy and random effects for the practices (ie, clusters). The results were presented as odds ratios (ORs) with 95% confidence intervals (CIs) based on the fixed effects. The change in the number of cigarettes per day between baseline and follow-up was compared between the groups using a mixed-effects linear regression model with the same random structure for the clusters. The mean difference in cigarettes per day between groups and 95% CI were reported. The corresponding estimated probabilities are presented as percentages of the outcomes in each group with 95% CIs. Analyses were performed using R (version 4.2.1; R Foundation for Statistical Computing), with packages "lme4" and "ggeffects."

PI is the preferred method for handling missing smoking status,[32] yet this conservative approach might introduce a risk of bias.[33–36] For example, PI may underestimate the effect in the study arm with the highest number of missing values.[33] Multiple imputation (MI) ensures that the variance of the combined estimates reflects the uncertainty of the imputation,[37] producing results that are less affected by the number of missing values and differences between groups.[33]

Secondary analyses for both primary and secondary outcomes were conducted. Initially, an analysis incorporating the imputation of missing values using MI (ie, assuming data missing at random) was performed. Multivariate imputation by chained equations with the "mice" package in R[37] was employed to impute missing responses within practices using two-level MI methods. This involved $m = 10$ imputed datasets and 30 iterations for each dataset. The results from the imputed datasets were pooled using Rubin's rules to estimate the strategy's effect, and were reported as ORs with 95% CIs for both primary and secondary outcomes. An analysis using only complete cases was performed following the same approach as for the primary analysis.

Several post hoc analyses were conducted. A per protocol analysis was performed comparing only those participants from the intervention group who were exposed to the strategy as intended (using the outcome: exposure to the stop-smoking strategy after the smear) to the control group. Subgroup analyses of the primary analysis for the primary outcome were conducted to explore who benefited most from the strategy. This included assessing whether women who were exposed to the strategy as intended (using the outcome: exposure to the stop-smoking strategy after the smear) or received stop-smoking advice during follow-up during another health care visit (using the outcome: exposure to stop-smoking advice delivered by health care professionals during another health care visit during follow-up; not part of the strategy) were likelier to undertake a quit attempt. Comparisons were also made between women smoking daily and non-daily.

Lastly, descriptive statistics for the psychological and behavioral measurements were reported.

Results

A total of 480 women who smoke participated in the study: 266 women were recruited from 37 practices in the intervention group, and 214 women were recruited from 38 practices in the control group (Figure 1). The 6-month measurements were completed by 80% of the participants in the intervention group and 86% of those in the control group, with no observed baseline differences between participants who did versus those who did not complete the primary outcome. The participants' baseline characteristics were balanced across both study groups (Table S1, Appendix 4).

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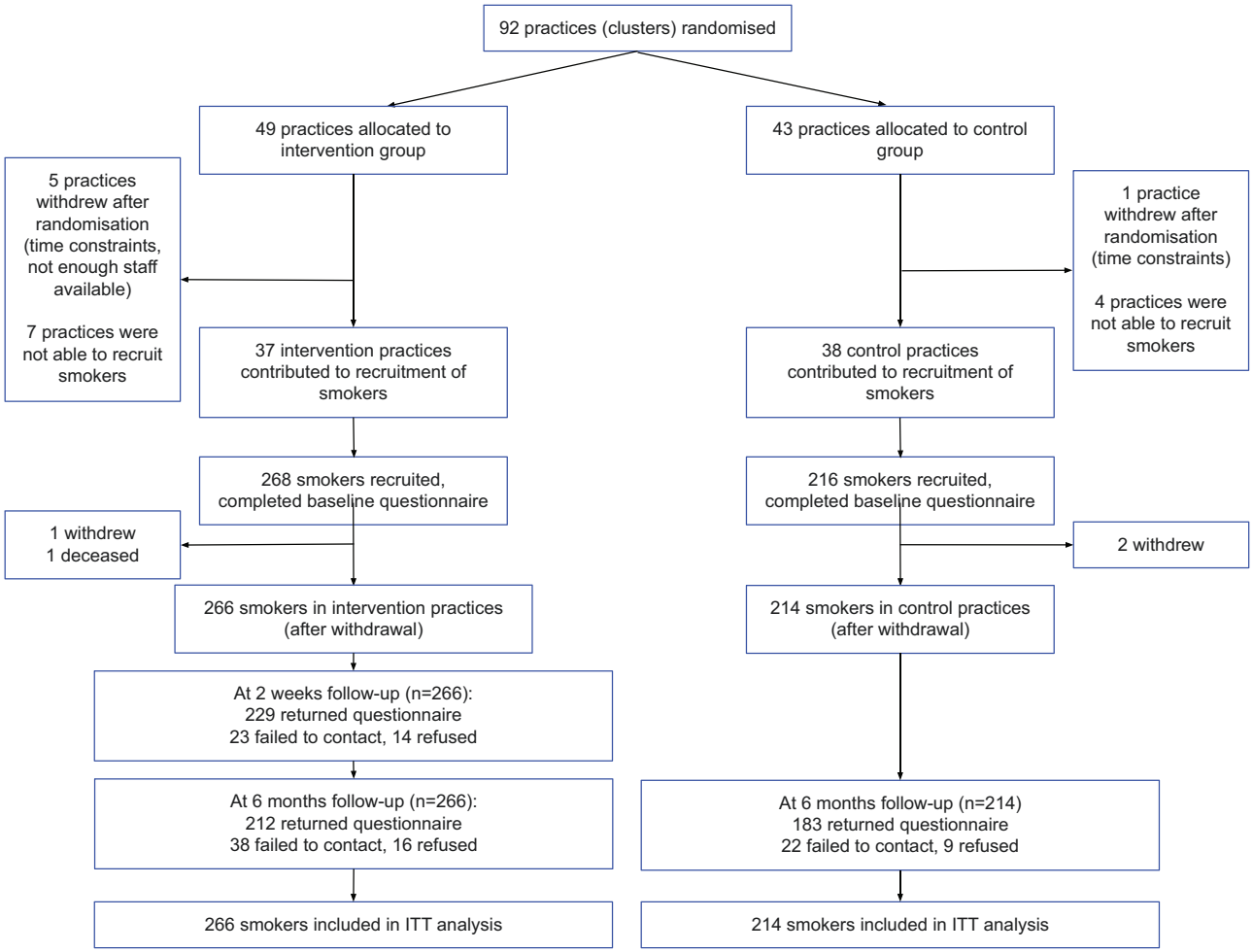

Figure 1. Flow diagram of the inclusion of general practices and women who smoke in the SUCCESS study. Abbreviations: ITT = intention-to-treat, *n* = number of participants, SUCCESS = smoking cessation strategy in the national cervical cancer screening program.

Primary Outcome

Table 1 indicates that the rates of undertaking a serious quit attempt of at least 24 hours within 6 months from baseline were similar between the intervention (39.8%) and control groups (36.0%), showing no significant difference in the odds of making a quit attempt, as analyzed using PI (with an ICC of 0.0066). Analyses using MI (ICC = 0.029) and complete cases (ICC = 0.032) also did not reveal a significant difference between the study groups. Comparing only those participants from the intervention group who received the stop-smoking strategy as intended (73.3%) to the control group showed a significant effect on making a quit attempt (OR 1.49 [1.01–2.22]).

Both analyses following intention-to-treat and per protocol show a direction of the point estimates in favor of the intervention group, where the MI, complete case, and per protocol analyses yielded a stronger yet less precise OR. Table S2 (Appendix 4) details the number of quit attempts according to the baseline motivational score.

Secondary Outcomes

The 7-day PPA at the 6-month follow-up did not significantly differ between the intervention (21.1%) and control groups (16.3%), as analyzed using PI. The MI and per protocol analyses showed a stronger point estimate, albeit nonsignificant and less precise, in favor of the intervention group. The complete case analysis showed a similar effect that did not significantly differ between the groups (Table 1).

The odds of having improved MTSS were similar between the intervention and control groups. Similarly, the reduction in the number of cigarettes smoked between the 6-month follow-up and baseline was comparable between both study groups. The secondary analyses (MI, complete cases, and per protocol) for an increase in motivation and reduction in the number of cigarettes smoked yielded results similar to the primary analysis, without significant differences between the study groups (Table 1).

Subgroup Analysis of the Primary Outcome

Within the intervention group, participants who received the strategy as intended following their smear test (encompassing brief advice containing the AAC steps) had significantly higher odds of making a serious quit attempt compared to those who were not exposed (OR = 2.69, 95% CI = 1.44–5.01) (Table 2). Exposure to stop-smoking advice by a PA during follow-up during another health care visit (spanning from after the strategy up to 6 months; not part of the strategy) was 19.9% in the intervention group versus 6.1% in the control group. This exposure was associated

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Table 1. Primary and Secondary Outcomes

	Quit attempt[a]	7-day PPA	MTSS	CPD T2-T1
Observed				
Intervention (n = 266): observed n (%) or mean (SD)	106 (39.9%)	59 (22.2%)	77 (29.0%)	−0.87 (SD 4.0)[b]
Control (n = 214): observed n (%) or mean (SD)	77 (36.0%)	37 (17.3%)	61 (28.5%)	−0.97 (SD 5.3)[b]
Percentages with CI				
Intervention: estimated probabilities (95% CI)[c]	39.8% (33.8–46.0)	21.1% (16.0–27.5)	29.0% (23.8–34.7)	−0.87 (−1.48 to −0.27)[d]
Control: estimated probabilities (95% CI)[c]	36.0% (29.7–42.8)	16.3% (11.3–22.8)	28.5% (22.9–34.9)	−0.96 (−1.62 to −0.30)[d]
Effect size				
$ITT_{penalized\ imputation}$ (n = 480): OR[e] (95% CI), p-value	1.18 (0.80–1.72), p = .41	1.38 (0.83–2.29), p = .21	1.02 (0.69–1.52), p = .92	0.09 (−1.62–0.99), p = .20
$ITT_{multiple\ imputation}$ (n = 480): OR[e] (95% CI), p-value	1.37 (0.91–2.08), p = .14	1.62 (0.96–2.75), p = .07	1.13 (0.72–1.78), p = .60	0.06 (−1.03–1.14), p = .92
Complete cases: OR[e] (95% CI), p-value	1.37 (0.88–2.12), p = .16[f]	1.59 (0.91–2.77), p = .11[f]	1.15 (0.72–1.85), p = .55[f]	0.04 (−1.08–1.16), p = .07[f]
$PP_{penalized\ imputation}$ (n = 409, intervention n = 195): OR[e] (95% CI), p-value	1.49 (1.01–2.22), p = .047	1.68 (0.96–2.95), p = .07	1.23 (0.80–1.87), p = .34	0.18 (−1.67–0.40), p = .73

Quit attempt = primary outcome: undertaking at least one serious quit attempt of at least 24 hours within 6 months from baseline.
7-day PPA = 7-day point prevalent abstinence (binomial; not having smoked in past 7 days coded as "1").
MTSS = increase in motivation to stop-smoking at follow-up compared to baseline (binomial, improvement coded as "1").
CPD T2-T1 = reduction in number of cigarettes smoked at follow-up compared to baseline (mean difference, continuous).
Abbreviations: ITT = intention-to-treat, OR = odds ratio, PP = per protocol.
[a]Binomial, quit attempt coded as "1."
[b]Mean CPD T2-T1.
[c]Estimated probabilities corresponding to the analysis with penalized imputation.
[d]Mean difference of cigarettes smoked per day between T2 and T1, with confidence intervals (CIs).
[e]Referent = control group.
[f]Number of observations for complete case analysis: Quit attempt: n = 395; Missings: 85 (54 intervention, 31 control), 7-day PPA: n = 394; Missings: 86 (55 intervention, 31 control), CPD T2-T1: n = 357; Missings: 123 (78 intervention, 45 control), MTSS: n = 371; Missings: 109 (67 intervention, 42 control).

with higher odds of making a quit attempt within the intervention group and significantly differed between the two study groups (OR = 4.30; 95% CI: 1.07–17.35). Both subgroup analyses showed a stronger effect on the primary outcome, but with wider CI compared to the primary analysis (Table 2).

There was no significant difference in the odds of making a quit attempt within 6 months from baseline between participants smoking daily versus non-daily in the two study groups (Table S3, Appendix 4).

Continuous Abstinence, 24-Hour PPA, and Other Psychological and Behavioral Measurements

Continuous abstinence at 6 months was observed in 6.4% of the participants in the intervention group versus 3.7% in the control group. Among participants who smoke daily, the 24-hour PPA at 6 months was similar between the intervention and control groups (Table 3).

In the intervention and control groups—16.2% versus 12.2%, respectively—used stop-smoking aids or support (eg, nicotine replacement therapy, medication, or professional counseling). In total, 14.7% of women from the intervention group were connected with professional smoking cessation counseling directly after their smear test with a higher number of follow-up appointments, compared to 6 women (2.8%) who received professional support in the control group (Table 3).

The other smoking-related measurements (number of relapses, smoking status of partner, and Heaviness of Smoking Index) were comparable between groups (Table S4, Appendix 4). Both the perceived general risk of developing cancer for a woman who continues smoking compared to one who quits or has never smoked, and the perceived personal risk of developing diseases related to smoking were comparable between groups. In both groups, the perceived personal risk was scored highest for lung cancer, and lowest for cervical cancer (Table S4, Appendix 4).

Discussion

Principal Findings

In this cluster-randomized controlled trial, a brief stop-smoking strategy delivered by PAs to women who smoke after cervical cancer screening did not significantly influence the odds of undertaking a serious quit attempt during a 6-month follow-up. Although nonsignificant, the odds of making a quit attempt or to be abstinent from smoking in the past 7 days were in favor of the intervention group, with a stronger effect observed in those participants who were indeed exposed to the strategy (73.3%). Between groups, no difference was observed in the reduction in cigarettes smoked per day or increase in motivation to stop. The uptake of professional counseling to stop-smoking was higher in the intervention group (14.7%) than in the control group (2.8%).

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Table 2. Quit Attempts Within the Intervention and Control Group

	Quit attempt[a] Subset: intervention $n = 266$	Quit attempt[a] Subset: control $n = 214$	Quit attempt[a] Interaction term $n = 480$
Exposed to Ask-Advise-Connect after the smear by the PA[b]			
Observed exposure: *n* (%)	195 (73.3%)	27 (12.6%)	222 (46.3%)
$ITT_{penalized\ imputation}$: OR (95% CI), *p*-value	2.69 (1.44–5.01), $p = .002$	2.13 (0.94–4.84), $p = .07$	1.27 (0.45–3.54), $p = .65$
Exposure to stop-smoking advice by a PA during follow-up[c]			
Observed exposure: *n* (%)	53 (19.9%)	13 (6.1%)	66 (13.8%)
$ITT_{penalized\ imputation}$: OR (95% CI), *p*-value	3.27 (1.71–6.27), $p \leq .001$	0.76 (0.22–2.62), $p = .67$	4.30 (1.07–17.35), $p = .04$
Exposed to stop-smoking advice by various health care professionals (including PAs)[d]			
Observed exposure: *n* (%)	88 (33.1%)	48 (22.4%)	136 (28.3%)
$ITT_{penalized\ imputation}$: OR (95% CI), *p*-value	3.59 (2.08–6.19), $p \leq .001$	2.38 (1.24–4.60), $p = .01$	1.50 (0.64–3.52), $p = .35$

Abbreviations: CI = confidence interval, ITT = intention-to-treat, OR = odds ratio, PA = practice assistant.
[a]Quit attempt = primary outcome: undertaking at least one serious quit attempt of at least 24 hours within 6 months from baseline.
[b]Exposure to Ask-Advise-Connect after the cervical smear directly after baseline, with exposure = 1; assessed in participants of the intervention group 2 weeks after the smear; potential exposure in the control group was measured at 6 months; OR referent = not exposed.
[c]Exposure to stop-smoking advice by a PA in the period after the intervention up to 6 months, with exposure = 1; assessed in both intervention and control group; OR referent = not exposed.
[d]Exposure to stop-smoking advice by various health care professionals in the period after the intervention up to 6 months, with exposure = 1; OR referent = not exposed.

Strengths and Limitations

This study adopted a novel and practical approach to encourage women who smoke to stop-smoking at an age when the prevalence of smoking-related diseases is still low. This trial is the first to utilize the AAC method within a strategy involving brief advice delivered by PAs to cervical screening participants in a general practice setting. The pragmatic approach and the demographics of our study sample enhance the applicability of our results to daily practice care. One-third of the participants were smoking non-daily at baseline, which is comparable to the distribution among Dutch women or adults—although the proportion of those who smoke daily increases with age.[22] In addition, only 1.5% of participants exhibited high nicotine dependence, aligning with the 1.8% of Dutch women classified as heavy smokers.[22] With a mean age of 44.7 years (SD 10.2), this study sample was representative of cervical cancer screening participants.[23] Approximately, 15% of the participants possessed low educational levels (compared to 25.8% among Dutch adults).[38] Only 15.1% reported a non-Dutch background. Recent demographics of cervical screening participants in the Netherlands are not available; however, it is known that individuals with a lower educational level or a migrant background are less likely to participate in such studies.[39] Overall, our data provide new insights into the demographics of smoking among women visiting their general practice (GP) for cervical screening. In behavior change interventions, blinding participants to the nature of the intervention can be challenging.

The recruitment challenges during the coronavirus disease 2019 (COVID-19) pandemic meant that statistical power was not achieved. Consequently, we cannot conclusively determine whether women who smoke benefitted from this stop-smoking strategy. Nonetheless, both primary and secondary analyses for the primary outcome indicated effect sizes that favored the intervention group, with corresponding CIs. The observed percentages and estimated probabilities for both the primary outcome and the secondary outcome of the 7-day PPA were in favor of the intervention group. Using the per protocol analysis, the intervention showed a borderline significant effect on the performance of a serious quit attempt, but these results should be interpreted with reserve as they can be subject to selection bias. Analyses using MI and per protocol revealed a more pronounced difference in the 7-day PPA between the groups. For MI, this discrepancy could be attributed to the absence of a cluster effect in MI, or because MI is less conservative and less sensitive to differences in the number of missing values between groups.[33] Although imputing clustered data poses challenges, we consider the use of MI in our study to be representative. With PI, the variability between clusters was almost eliminated (ICC = 0.0066). In contrast, with MI, the ICC for the primary outcome (0.029) was closer to that observed in complete cases (0.032), suggesting that MI results might more reliably reflect the intervention effect. Furthermore, women who smoke might be less reluctant to report a quit attempt compared to actual smoking cessation, as unassisted quit attempts are often underreported compared to assisted attempts.[40] This could lead to an underestimation of the strategy's effect when using PI. In the future, we expect that MI methods will become more prevalent in handling missing smoking cessation outcomes.[33–36] Within the intervention group, almost a quarter of participants reported not to have been exposed to the strategy's AAC steps after the cervical smear. On the other hand, participants who were exposed to the strategy as intended (compared to unexposed participants) or to advice from a PA during another health care visit after the smear seemed likelier to attempt quitting. In a PE, we will assess what factors related to the general practices could explain why participants did or did not receive the strategy as intended and what could be done to support an adequate implementation of the strategy.[26]

The recruitment of both practices and participants was more time-consuming than anticipated, mainly due to the COVID-19 pandemic. For the primary outcome, no biochemical validation was used, as the strategy is considered a low-demand intervention[41,42] and selection bias could occur if the participants were informed about a biochemical validation

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Table 3. Smoking-Related Measurements, Exposure to Advice and Use of Smoking Cessation Support

	Intervention (*n* = 266)	Control (*n* = 214)	Total (*n* = 480)
Smoking-related measurements			
6 months continuous abstinence (% with 95% CI)[b]	17 (6.4%, 4.0–10.0)	8 (3.7%, 1.9–7.3)	25 (5.2%)
24-hour PPA in women who smoke daily (% with 95% CI)[a]	28 (15.5%, 10.9–21.5) of *n* = 181	20 (13.2%, 8.7–19.6) of *n* = 151	48 (14.5%) of *n* = 332
Exposure to advice			
Exposed to stop-smoking advice by health care professionals, *n* (%)[c]			
Practice assistant	53 (19.9%)	13 (6.1%)	66 (13.8%)
Practice nurse	28 (10.5%)	8 (3.7%)	36 (7.5%)
General practitioner	15 (5.6%)	14 (6.5%)	29 (6.0%)
Dentist	4 (1.5%)	9 (4.2%)	13 (2.7%)
Medical specialist	6 (2.3%)	10 (4.7%)	16 (3.3%)
Midwife	1 (0.4%)	0	1 (0.2%)
Physiotherapist	2 (0.8%)	0	2 (0.4%)
Other professional	6 (2.3%)	3 (1.4%)	9 (1.9%)
Number of professionals whom advice was received, *n* (%)			
1	65 (24.4%)	40 (18.7%)	105 (21.9%)
2	19 (7.1%)	7 (3.3%)	26 (5.2%)
3	4 (1.5%)	1 (0.5%)	5 (1.0%)
Use of smoking cessation support			
Connected to support directly after the smear, *n* (%)[d]	37 (13.9%)	—	—
Received professional support within the practice, *n* (%)[d]	39 (14.7%)	6 (2.8%)	45 (9.4%)
Used stop-smoking aids/support, *n* (%)[e]	43 (16.2%)	26 (12.2%)	69 (14.4%)
Type of aids/support used, *n* (%)			
Nicotine Replacement Therapy	17 (6.4%)	15 (7.0%)	32 (6.7%)
Medication	13 (4.9%)	3 (1.4%)	16 (3.3%)
Course	1 (0.4%)	1 (0.5%)	2 (0.4%)
Practice nurse	13 (4.9%)	3 (1.4%)	16 (3.3%)
Psychologist	2 (0.8%)	0	2 (0.4%)
Group	1 (0.4%)	1 (0.5%)	2 (0.4%)
Other[e]	8 (3.0%)	9 (4.2%)	17 (3.5%)
Appointments for professional support to stop-smoking			
Number of appointments, mean (SD)	3.7 (2.2)	2.0 (0.9)	3.3 (2.1)
≥1 follow-up appointment(s), *n* (%)	21 (7.9%)	6 (2.8%)	27 (5.6%)
Sought help on own initiative, *n* (%)	3 (1.1%)	2 (0.9%)	5 (1.0%)
Sought help elsewhere, *n* (%)	1 (0.4%)	3 (1.4%)	4 (0.8%)

Abbreviation: CI = confidence interval.
[a]24-hour PPA = 24-hour point prevalent abstinence (not having smoked in the past 24 hours).
[b]6 months continuous abstinence = not having smoked in the past 6 months.
[c]Exposure to stop-smoking advice by various health care professionals from the period after the intervention up to 6 months; multiple answers possible.
[d]Appointments within the general practice for professional support to stop-smoking.
[e]Other types of support used: apps *n* = 2, quit line *n* = 2, e-cigarette *n* = 2.

test before giving informed consent. At baseline, 50% of the participants in the intervention group (vs. 43.9% in the control group) had attempted to quit in the past 6 months, which is higher than the average of 34%–36% of Dutch people who smoke and attempted to quit in 2016 and 2022.[22,28] Introducing a 10% difference in quit attempts compared to the control group, as calculated in the sample size, might have been more challenging than anticipated. Alternatively, the high percentage of quit attempts at baseline could indicate that cervical screening participants are more engaged in their health compared to the general population, despite their use of tobacco. The participants from the intervention group received an additional questionnaire at the 2-week follow-up for the PE. Through quantitative and qualitative methods, this PE will assess whether this additional questionnaire influenced smoking cessation outcomes.[26]

Comparison With the Existing Literature

Smoking cessation among cervical cancer screening participants was previously evaluated in three studies.[43–45] These studies did not define how missing smoking cessation outcomes were handled, as only complete case analyses were conducted.[43–45] We contribute to this body of literature with a more robust methodology and evaluation of the effectiveness of a stop-smoking strategy in cervical screening participants.

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McBride et al. targeted women based on their pap smear results; women randomized to the intervention arm (n = 288) received a self-help cessation kit by mail, along with up to three telephone calls.[43] No significant difference in 7-day PPA, number of quit attempts, or continued abstinence was observed (even among women with aberrant smear test results) compared to women receiving usual care (n = 292) at 6 and 15 months follow-up.[43] Unlike McBride's findings, our study demonstrated greater differences in the percentages and estimated probabilities for the performance of a quit attempt, 7-day PPA, and continuous abstinence in favor of the intervention group. A possible reason might be that McBride et al. did not utilize the smear appointment as a teachable moment and that there was no interaction between care providers and patients.[17,29]

Hall et al. and Gorini et al. both integrated the smear test appointment with a smoking cessation intervention, which was delivered by nurses in [44] and midwives in [45]. The trial by Hall et al.[44] showed the most similarities in study design and setting with our trial. This exploratory trial revealed no difference in smoking abstinence between groups (n = 121 in each arm), but an improvement in the intention to stop-smoking at 10 weeks among women who received the intervention. The study explicitly targeted women who smoke, which could have introduced selection bias, and the follow-up period was relatively short, with measurements taken at 2 and 10 weeks.[44] In contrast, our results might be more applicable to daily care because the participants were unaware of the true aim of the trial when receiving the strategy.

In the trial by Gorini et al., women in the intervention arms received a self-help booklet for cessation, alongside smoking cessation counseling tailored to their stage of change (n = 363). For one of the two treatment arms, this was combined with physical activity counseling (n = 366) (controls n = 371). Women in the preparation stage were twice as likely to quit smoking compared to controls; however, women in the precontemplation stage were less likely to quit than their controls.[45] In our trial, the increase in motivation to stop did not vary between the treatment groups. The observed percentage of participants making a serious quit attempt was higher among those with a higher MTSS baseline score, which aligns with the expectation that motivation to stop predicts quit attempts.[46] Unlike Gorini et al., we observed within our intervention group that a higher percentage of the participants with a low-to-moderate baseline MTSS score made a quit attempt compared to the controls.

Unassisted quit rates are estimated to be 2%–3%, with brief stop-smoking advice received from a physician potentially adding another 1%–3%.[9] In our trial, 3.7% of the controls reported continuous abstinence compared to 6.4% of the participants in the intervention group. Training GPs in smoking cessation care led to similar, nonsignificant results for 7-day PPA and continuous abstinence in people who smoke.[47] Notably, in our study, the number of participants who were connected to professional support within the practice was remarkably higher compared to the controls, with 39 (14.7%) versus 6 (2.8%) participants, suggesting a benefit in proactively offering support to stop-smoking after the smear. This is relevant, as individual counseling has been shown to support people who smoke in quitting.[48] In the PE, we will study the active components of the strategy, counseling, or context that contributed to stopping smoking.[26] For nurse-led smoking cessation interventions, evidence does not suggest that the effect of support varies by patient group.[10] This might also apply to PAs, as previous studies have demonstrated the potential of PAs in delivering stop-smoking care in various settings and patient groups.[49,50]

Conclusion

A brief stop-smoking strategy delivered by PAs to women who smoke and attend their general practice for a cervical cancer screening did not significantly increase the likelihood of making a serious quit attempt during a 6-month follow-up. Nonetheless, the effect of the strategy on undertaking a quit attempt and on the 7-day point prevalent abstinence was in favor of those women who received the strategy as intended. Additionally, a higher uptake of professional counseling for smoking cessation was seen in women who received the strategy. These findings may indicate that such a brief strategy could be a valuable addition to daily general practice care for reaching women who smoke. The PE will further examine the feasibility, acceptability, and implementation process of this strategy. The outcomes of this trial, alongside the insights from the PE, could inform clinical practices within cervical cancer screening programs or health care settings in which PAs are routinely engaged in behavior change consultations.

Supplementary Material

Supplementary material is available at *Nicotine and Tobacco Research* online.

Funding

This project was funded by a grant from the Dutch Cancer Society (UVA 2015-7853).

Declaration of Interests

None declared.

Acknowledgments

We wish to thank the study participants and health care professionals who participated in this study. We wish to thank S. Königs for training practice assistants. We also wish to thank E. Sert and S. de Graaf for their support in data collection and data management, as well as masters students A. van der Zandt and E. Hartsema for recruitment of participating practices and data entry. We wish to thank W. Busschers for their support in statistical data analysis.

Author Contributions

Marthe B.L. Mansour (Conceptualization [equal], Data curation [equal], Formal analysis [equal], Investigation [equal], Methodology [equal], Writing—original draft [equal], Writing—review & editing [equal]), Mathilde R. Crone (Conceptualization [equal], Formal analysis [supporting], Funding acquisition [equal], Investigation [supporting], Methodology [equal], Supervision [equal], Writing—review & editing [supporting]), Henk C. van Weert (Conceptualization

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Clinical Trial Registration

Trial registration number NL5052 (NTR7451) was registered in the Dutch Trial Register on September 9, 2018.

Data Availability

Data not publicly available. The data underlying this article will be shared on reasonable request to the corresponding author.

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