"Appagalo" a Customized Mobile Health Intervention (mHealth) for Smoking Cessation in Women: A Randomized Controlled Trial

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ABSTRACT

BACKGROUND: Almost 30% of Chilean women report cigarette smoking with important repercussions on their health.

OBJECTIVE: Design and test a mobile phone intervention for smoking cessation in young women.

STUDY DESIGN: A mobile application (app) was created using the best available evidence and consumer input. Its effectiveness was assessed through a randomized clinical trial.

STUDY PARTICIPANTS: Women 18 to 44 years old from middle-class neighborhoods in Santiago, Chile. Inclusion criteria were intention to quit cigarette smoking in the following month and having a smartphone cell phone. Women with positive screening for risky alcohol consumption were excluded.

INTERVENTION: App with content to support cigarette smoking cessation over 6 months. The control arm included an app that delivered general messages to promote permanence in the study. Telephone follow-up was performed at 6 weeks, and at 3 and 6 months after randomization.

MAIN OUTCOME MEASURE: No smoking in the past 7 days at 6 weeks from enrolment. Intention-to-treat analysis was carried out using SPSS 17.0 with a significance level set at .05.

RESULTS: 309 women entered the study. Mean number of cigarettes smoked in a day was 8.8. 58.6% of the participants (n = 181) completed the follow-up for the primary outcome. With intention-to-treat analysis, 9.7% of participants in the intervention group reported not having smoked any cigarettes in the last 7 days vs 3.2% in the control group (RR 2.98 CI 95% 1.11-8.0, $P = .022$). Additionally, 12.3% vs 1.9% of the participants in the intervention group and control group reported continuous abstinence at 6 weeks, respectively (RR 6.29 95% CI 1.9-20.8, $P < .001$). Continuous abstinence was also significant at 6 months (P-value of .036).

CONCLUSIONS: The "Appagalo" app is an effective tool to support smoking cessation in young women. It is a simple mHealth alternative for smoking cessation that can contribute to improving women's health in the Americas and worldwide.

KEYWORDS: smoking cessation, telemedicine, cellphones, women's health, mHealth, cancer prevention

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Introduction

Smoking is the leading cause of preventable deaths around the world. One billion adults smoke worldwide and of them, half will die prematurely from tobacco-related diseases, losing an average of 10 to 15 years of life.[1,2]

Eighty percent of deaths caused by tobacco occur in low or middle-income countries.[1]

Although between 2011 and 2017 prevalence of smoking in Chile decreased, importantly, 33.3% of the population 15 years or over reports currently smoking, either occasionally or daily[3,4]

and the mean number of cigarettes smoked daily in the country is 10.4 cigarettes/day.[5]

Cigarette smoking in women has become a problem worldwide. A systematic review by Jafari et al in 2021 reported a global prevalence of 28% of ever smokers and 17% of current female smokers.[6] Chilean women are among the highest smokers in the region, with a smoking prevalence of 29.1% (reported occasionally or daily). Importantly, 19.7% of women declare smoking cigarettes daily.[4]

Smoking patterns in women differ significantly from men's. Women tend to smoke fewer cigarettes a day, they favor filtered cigarettes, cigarettes low in tobacco and they don't usually smoke self-rolled cigarettes, nor cigars or pipes.[7]

In women, smoking increases the risk of ovarian and cervical cancer, early menopause, and infertility.[7,8] Additionally, women of childbearing age have the potential to become pregnant smokers. In Chile, it is estimated that at least 1 in 4 women fails to quit smoking during pregnancy.[8,9] This is associated with important reproductive consequences for the mother and the child.[8] On the other hand, newborns and infants of smoking mothers are at greater risk of sudden infant death, greater risk of developing asthma, and greater morbidity and mortality due to respiratory diseases in childhood.[10,11] Overall, infant morbidity and mortality attributable to prenatal smoking in Chile are high.[12]

Children of all ages are an important group exposed to secondhand smoke by smoking mothers, with deleterious effects on their health from an early age, and with behavioral modeling that doubles the probability that the child will become a smoker.[10,11]

Smoking cessation is a complex process that involves the integration of physical, psychological, and social aspects. The World Health Organization, through their MPOWER strategy (**M**onitor tobacco use; **P**rotecting people from tobacco smoke; **O**ffer help to quit tobacco; **W**arn about dangers of tobacco; **E**nforce bans on tobacco advertising, promotion and sponsorship; and **R**aise taxes on tobacco), identifies smoking cessation support as 1 of the 6 most important and cost-effective measures for tobacco control yet it is rarely prioritized at the policy level.[13] Mobile technologies have increased exponentially in the last decade,[14] and so the growing use of mobile technologies (mHealth) emerges as a low-cost, wide coverage alternative to support smokers to quit.[15] In Chile, over 80% of households have access to a mobile phone device (97% and 82.8% for families of high and low socioeconomic status, respectively).[16] Mobile technologies are attractive to the user because they can access them at any time, from a variety of places, and anonymously.[15] mHealth strategies contribute to reaching sectors of the population that generally do not go to health services, much less for preventive actions. International studies have demonstrated the effectiveness of mHealth interventions in support of smoking cessation, doubling the proportion of subjects who quit smoking.[17-20] A study by Free et al[17] highlighted that a text messaging intervention doubled the probability of withdrawal from tobacco at 6 months (10.7% in the intervention group vs 4.9% in the control group, RR 2.2 95% CI 1.8-2.68, $P < .0001$). There is also increasing evidence regarding the cost-effectiveness of these interventions[21,22] and yet, the availability of an effective, culturally tailored smoking cessation App for Latina populations is lacking.

The purpose of the present study was to design and evaluate a mHealth intervention to support cigarette smoking cessation in women of childbearing age in Chile.

Methods

Study Participants

We recruited women between 18 and 44 years of 2 middle-income areas of the Chilean capital city of Santiago: Puente Alto and La Florida from Sept 2017 to March 2018.

Inclusion and Exclusion Criteria

Inclusion criteria were: 18-44 years of age; having consumed >=100 cigarettes in the lifetime and >=7 cigarettes per week during the last 6 months; intention to quit smoking in the following month and having a smartphone with Android operating system. Intention to quit was assessed by asking potential participants the following question through a telephone survey: Do you want to try to quit smoking in the next month?. We excluded women who were planning to change their residence within the next year and women with positive screening for risky alcohol consumption.

Sampling Method and Recruitment

The study was publicized through posters in health centers, public spaces, and social networks. Women interested in the study filled out an online form, and those who met the basic requirements of the study (age and area of residence) were contacted by research assistants, who applied a telephone survey on sociodemographic, clinical, and smoking habits variables, and evaluated the criteria of study eligibility. All eligible women were invited to download the app (either intervention or control app) and signed informed consent in the app. Those who signed informed consent received the contents of the app, according to the allocated arm. All information was entered into a university licensed Research Electronic Data Capture (REDCap) platform.[23] As its developers state: "REDCap is a secure web application for building and managing online surveys and databases, designed to support data capture for research studies".[24]

Intervention Design

The study had an initial qualitative phase, which contributed to inform the design of the app, followed by a randomized

clinical trial (RCT) to evaluate the effectiveness of the intervention. The results of the qualitative study have been published elsewhere.[25]

Randomization Sequence and Masking

We conducted a two-arm RCT, in which the effectiveness of a smoking cessation intervention was evaluated based on an application (app) for mobile phones vs a control group. Eligible participants were randomized to the intervention group or to the control group using an automated and computerized process, in blocks of 6. A minimization algorithm was used to balance the level of nicotine dependence between the study groups, according to the Fagerstrom test score (≤5 or> 5) at study entry.

Participants were not told which study group they were assigned to, but due to the nature of the intervention we considered them not blind.

All researchers who gathered and analyzed outcome data were masked to treatment allocation.

Intervention Description

The intervention app sent a sequence of motivational messages and tips to help participants to prepare for quitting smoking during the next 2 weeks, including the request that the participant set a date to quit smoking (D-Day). The intervention app sent an average of 4 messages per day during the first month, followed by 3 messages per week until the end of the study (6 months). The messages included motivational content, advice on stress management, how to request support from friends and family, how to use relaxation and distraction techniques, and how to deal with anxiety, sporadic consumption, and early relapse. A "money saving" calculator was included due to results of our qualitative study. Also, a "help button" sent additional messages in case the participant experienced nicotine cravings.[25] Additionally, a button was created for sporadic consumption or possible relapse, with the aim of providing support and new strategies in case the participant had returned to smoking. During the first month after D-Day, participants received a question every night about whether they had smoked or not, from which the app generated a positive reinforcement message through achievement labels, which were deployed in a staggered manner as the participant added days without smoking. A detailed description of the intervention app is available in the Appendix.

The control group received an application similar to the intervention app, but without content to support smoking cessation. Both versions of the app had a technical support button.

Study participants did not receive any financial compensation. To increase retention, all participants were informed that they would participate in a prize draw after answering the 6-month follow-up questionnaire.

Statistical Analysis

The data from the randomized clinical study were analyzed by intention-to-treat (ITT) for the outcomes related to the effectiveness of the intervention at 6 weeks, and at 3 and 6 months after randomization in the study groups. Analogous results were carried out on an available cases (AC) analysis scheme.

Differences in baseline variables between intervention and control groups were assessed using t-tests for numerical variables and Chi-squared tests for categorical variables.

Differences in outcomes among groups were evaluated using chi-squared tests along with relative risk and its 95% confidence interval (95%CI) to account for the effect measure. The number needed to treat (NNT), with its 95% CI was added to measure the impact of the intervention

The analysis was performed for the entire sample and also for age subgroups, nicotine addiction (Fagerstrom score ≤5,> 5), and educational level (<8 years, 8-12 years, ≥ 12 years).

Sample size. The sample size was calculated based on previous studies. 28% quitting in the intervention group and 13% in the control group were expected. To achieve 90% power with a significance level of 0,05 (2-sided tests) and considering a 20% attrition for the 6-month follow-up evaluation, a sample size of 400 women was needed.

Follow-Up

Attempts to contact participants were made by telephone, WhatsApp messages and email at 6 weeks, 3 months and 6 months. Those participants who could not be reached after ten attempts on different days and times were considered lost to follow-up.

Outcome Definitions. According to international literature, we defined our main variable for abstinence as "no smoking in past 7 days". Also, "continued abstinence" was defined as having smoked 5 cigarettes or less in each specific time period.

(1). Primary Outcome

(a) The proportion of women who self-reported not smoking during the last 7 days at 6 weeks from randomization day.

(2). Secondary outcomes

(a) The proportion of women who self-reported not smoking during the last 7 days, at 3 and 6 months.
(b) The proportion of women who self-reported not having smoked continuously (continuous abstinence) at 6 weeks, and at 3 and 6 months.
(c) The proportion of women who reported a reduction of at least 50% in the number of cigarettes smoked at 6 months.

(3). Adverse effects:

(a) The proportion of women who reported osteotendon injuries of the hand during the use of mobile technology throughout the study (measurement at 6 months).
(b) The proportion of women who reported having been involved in traffic accidents during the study period (measurement at 6 months).

(4). Use of co-interventions:

(a) The proportion of women who reported having used any other strategy to support smoking cessation during the study (measurement at 6 months).

IRB Approval. This study was approved by the Ethical-Scientific Committees of the Southeast Metropolitan Health Service and the Faculty of Medicine of the Pontificia Universidad Católica de Chile.

Results

Formative Qualitative Phase

The qualitative phase of the study included 9 Chilean women between 18 and 44 years old, smokers of ≥7 cigarettes a week, with the intention to quit smoking. Through thematic analysis,[26] 5 central themes were identified: a. Patterns of cell phone use, Internet and mobile applications, b. Facilitators and barriers to intervention; characteristics of tobacco consumption and motivations to be addressed by the app, c. Specific contents to include in the app, d. Women's preferences on the name, logo, and format of the app. The research team worked with experts in design and digital communications to integrate these concepts into the design of the app. The qualitative study is available in full elsewhere.[25] A visualization of the app can be found in Appendix Figures A1 and A2.

Recruitment and Descriptive Analysis

We evaluated 602 women for eligibility from September 2017 to March 2018.

435 were eligible and we randomized 403. Three hundred and nine women were finally included in the study. Thirty-two eligible women were not randomized, because they required more than 1 phone call to complete the eligibility assessment and could not be reached for the randomization times of the study. Of the 403 eligible women who were randomized, and an account was created to download the app, there were 94 who, despite sending the App download information through several channels, did not download the app and, therefore, they did not sign the informed consent that was the first step of the study. In those cases, it was not possible to establish contact with the participants again, and therefore, they were not included in the study.

We randomized 155 women to the intervention arm and 154 to the control arm. For the primary outcome, loss to follow-up was 75 (48.4%) in the intervention arm, and 53 (34.4%) in the control arm.

Figure 1 shows the study flow diagram.

Reasons for ineligibility are shown in Appendix Table A1.

During follow-up, 28 participants withdrew consent for the study (Appendix Table A2). The rest of the losses to follow-up correspond to women who could not be contacted by phone or email.

Table 1 shows the baseline characteristics of the 309 participants who entered the study. The control (n = 154) and intervention (n = 155) groups were similar in sociodemographic variables such as age (31.6 ± 6.9 and 32.9 ± 7.1 years respectively) and educational level. Likewise, both groups were comparable regarding smoking habits such as level of physical dependence on nicotine and number of previous attempts to quit smoking.

Effectiveness Outcomes

Of the 309 participants who entered the clinical study, it was possible to contact 181 for the 6-week follow-up milestone since randomization, which is equivalent to a global follow-up of 58.6% (65.6% in the control and 51. 6% in the intervention group).

All clinical effectiveness results were based on the available cases (AC) and on an intention-to-treat (ITT) analysis. (Table 2)

In the ITT analysis, the worst-case scenario was assumed, that is, that all participants without follow-up information continued to smoke.

In ITT analysis, the use of the APPAGALO mobile App showed that 9,7% (IC95% = [5,0 – 14,4]) of women in the intervention group and 3,2% (IC95% = [0,4 – 6,0]) in the control group reported they did not smoke in past 7 days. This is, the intervention tripled the chances of no smoking in the past 7 days at 6 weeks (primary outcome of the study), compared to the control App (OR = 3.0; 95%CI = [1.1 – 8.0]). Similarly, the APPAGALO mobile App increased by more than 6 times the chances of achieving continuous tobacco abstinence at 6 weeks (OR = 6.3; 95%CI = [1.9 – 20.8]) compared to the control App. For clinical effectiveness outcomes at 3 and 6-months follow-up, we got responses to the follow-up survey from 110 participants at 3 months (35.6%) and 59 participants at 6 months (19%). Due to the high number of women lost to follow-up, results for not smoking at 7 days at 3 and 6 months were not statistically significant. Nonetheless, even with the increased loss to follow-up, the App was effective at improving continuous abstinence in the 6-month ITT analysis, with a *P*-value of .036.

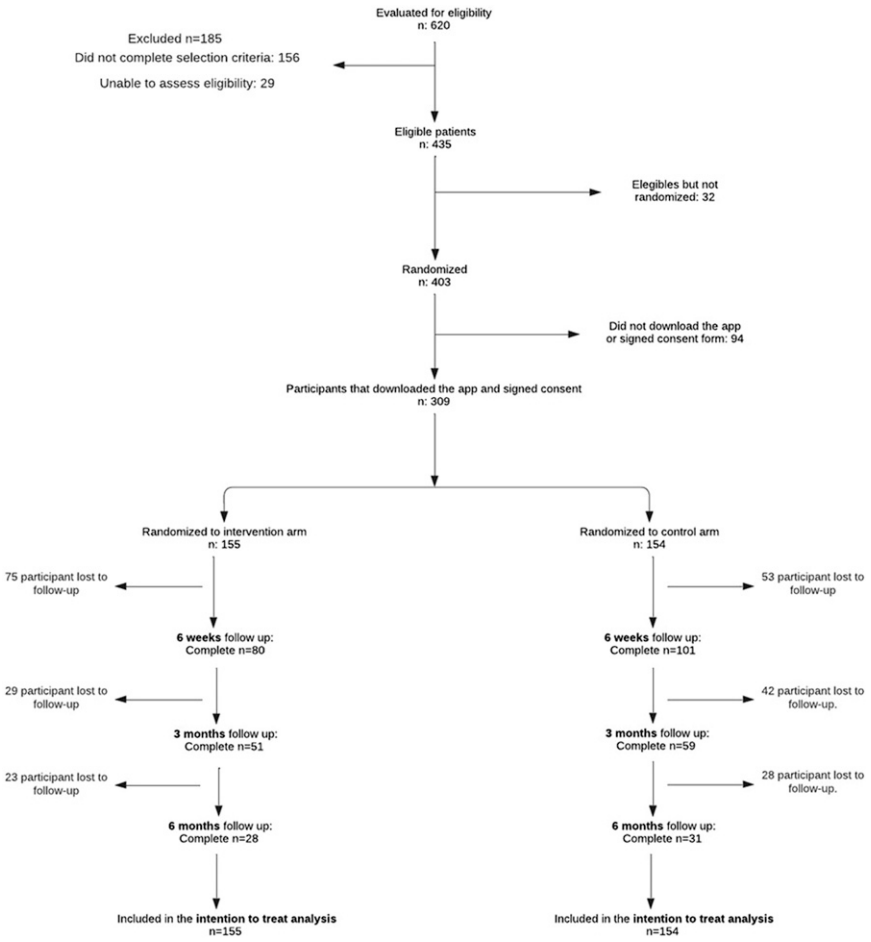

Figure 1. Eligibility and follow-up flow diagram Appagalo Study. Attempts to contact participants were made by telephone, WhatsApp messages, and email at 6 weeks, 3 and 6 months. Those participants who could not be reached after ten attempts on different days and times were considered lost to follow-up.

Importantly, only 16 women (NNT = 15.4, 95%CI = [8.4-100.0]) would have to download the App for 1 woman to stop smoking at 6 weeks. Similarly, 10 and 22 women (NNT = 9.62, 95%CI = [6.26-21.28] and NNT = 21.74, 95%CI = [12.17-123.46]) would have to download the App for 1 more woman to achieve continuous abstinence at 3 months and 6 months respectively. Analogous analyzes for AC is shown in Appendix Table A3.

Women in the intervention group smoked fewer cigarettes than those in the control group, with 28.6% (95%CI = [11,9 – 45,3]) of them reporting having smoked 0 cigarettes during the previous 7 days at 6 month follow-up in the former group vs 6,5% (95%CI = [0 – 15,0]) in the latter (*P*-value .008) (Appendix Table A4).

At 6 months, 60.3% of all women decreased their consumption by at least 50%, (with 71.4% participants in the intervention group compared to 50% in the control group, $P = .096$).

Subgroups Analysis

Analysis by Subgroups of Age at 6 weeks

Participants from 18 to 29 years old (38.5% of the total) and those from 30 to 45 years old (61.5% of the total) were analyzed separately.

In the ITT analysis, a difference was observed in favor of the intervention group for continuous abstinence in the youngest subgroup (0% in the control group vs 17.9% in the intervention group, $P < .001$). However this difference was lost at the 6 month follow-up. In the subgroup of women between 30 and 45 years, a trend in favor of the intervention group was observed for continuous abstinence, but it did not reach statistical significance (3.3% in the control group vs 9.1% in the intervention group, $P = .137$). No difference was observed between groups for no smoking in the past 7 days.

Analysis by Subgroups of Educational Level at 6 weeks

We analyzed results by educational level at 6 weeks. Participants of low educational level (up to 8 years of complete studies) were 2.7% of the total. Those of medium educational level (9-12 years of complete studies) comprised 38.4% of participants those with a high educational level (> 12 years of complete studies) were 58.8%.

In the subgroup of > 12 years of study, favorable results were observed for the intervention in all the analyzes by intention to treat (1.1% vs 10.7% of no smoking in the past 7 days in the control group and intervention group, respectively, $P = .008$). This difference was lost at 6 months follow-up.

We observed, 2.2% continuous abstinence in the control group vs 14.3% in the intervention group, $P = .004$. In the low

Table 1. Baseline characteristics of the APPAGALO study participants.

	INTERVENTION (N = 155)	CONTROL (N = 154)	TOTAL (N = 309)
Age (years); mean ± SD	32.9 ± 7.1	31.6 ± 6.9	32.3 ± 7.0
Age (years); %			
18-24	17.5	12.9	15.2
25-34	44.8	41.3	43.0
35-45	37.7	45.8	41.7
Education (years); mean ± SD	13.6 ± 2.5	13.8 ± 2.7	13.7 ± 2.6
Education (years); %			
<12	11.2	9.9	10.5
>=12	88.8	90.1	89.5
Nationality; %			
Chilean	99.3	98.1	98.7
Other	0.7	1.9	1.3
Previous attempts to quit smoking[a]; mean ± SD	2.9 ± 2.8	3.0 ± 2.4	2.9 ± 2.6
Previous attempts to quit smoking; %			
None	47.7	53.9	50.8
1-5 times	48.4	40.9	44.7
More than 5 times	3.9	5.2	4.5
Average number of cigarettes smoked in a day; mean ± SD	8.8 ± 6.5	8.7 ± 7.1	
Fagerstrom Score; mean ± SD	3.0 ± 2.4	3.1 ± 2.5	3.0 ± 2.4
Fagerstrom Score; %			
<=5	79.4	79.9	79.6
>5	20.6	20.1	20.4
Health Insurance; %			
Public	85.6	80	82.8
Private	11.8	15.5	13.6
Other	2.6	4.5	3.6

P values for numerical variables were obtained using t-Student test for independent samples or Pearson´s Chi-Squared test for categorical variables.
[a]Previous attempts to quit smoking were calculated excluding those who had never tried to quit smoking.

Table 2. Intention-to-treat clinical effectiveness outcomes of the APPAGALO study.

	INTERVENTION N(%)	CONTROL N(%)	RR (95% CI)	*P* VALUE
Six-weeks	(n = 155)	(n = 154)		
No smoking in past 7 days	15(9.7)	5(3.2)	**2.98 (1.11 - 8.00)**	**.022**
Continuous abstinence	19(12.3)	3(1.9)	**6.29 (1.90 - 20.83)**	**<.001**
Three-months	(n = 155)	(n = 154)		
No smoking in past 7 days	12(7.7)	15(9.7)	0,79 (0,38 - 1,64)	.534
Continuous abstinence	11 (7.1)	12(7.8)	0,91 (0,41 - 2,00)	.816
Six-months	(n = 155)	(n = 154)		
No smoking in past 7 days	8(5.2)	2(1.3)	3.97 (.86 - 18.4)	.104
Continuous abstinence	8(5.2)	1(.6)	**7.95 (1.01 - 62.8)**	**.036**

95%CI: 95% confidence interval; RR: relative risk. No smoking in past 7 days: self-reported abstinence in the last 7 days; Continuous abstinence: self-reported abstinence of less than 5 cigarettes during the whole study period.
P values were obtained using Pearson´s Chi-Squared tests.

and medium education subgroups, no significant differences were observed between the study groups.

Summary of findings is portrayed in Table 3.

Subgroup Analysis of Physical Dependence on Nicotine at 6 Weeks. Participants with low-moderate nicotine physical dependence (score of the Fagerstrom test up to 5) were 79.6% of the total. In the subgroup with low-moderate nicotine dependence, differences in favor of the intervention group were observed for both no smoking in the past 7 days (4.1% in the control group vs 11.4% in the intervention group, $P = .032$), and for continuous abstinence (2.4% in the control group vs 13.8% in the intervention group, $P = .002$). In the high nicotine dependence subgroup, as anticipated, it was not possible to demonstrate statistically significant differences between the groups nor in the 6 month follow-up. Table 3.

Analysis of Possible Adverse Effects and Co-interventions

Possible adverse effects associated with the intervention were evaluated at the 6-month follow-up milestone. Of the 42 participants with a 6-month follow-up, none reported having been involved in a traffic accident and no participants reported having hand injuries potentially associated with cell phone use throughout the study. Co-interventions were also measured at 6 months, highlighting that 2 participants in the control group reported having used an electronic cigarette or vaporizer during the study, compared to no participant in the intervention group. Only 1 participant in the control group reported using a smoking cessation medication during the study. (Appendix Table A4).

Discussion

Our study allowed the design of the first Chilean app to support smoking cessation in women of childbearing age and demonstrated its clinical effectiveness for both no smoking in the past 7 days and continuous abstinence at 6 weeks and 6 months under an intention-to-treat analysis.

Because smoking cessation is a process that usually includes relapses over time, it is expected that the results observed at 6 weeks correspond to the greatest difference in effect between the groups and a probable relapse at 3 months. Even if the only demonstrable effect of this intervention would have been observed at 6 weeks, it would have clinical and public health value by contributing to the fact that women have made a serious attempt to quit smoking, which brings them closer to definitive cessation. In fact, it is known that the greater the number of attempts to quit smoking in a smoker's life, the greater the chance that they will succeed in a subsequent attempt.[27]

Table 3. Clinical effective outcomes at 6 weeks stratified by age, nicotine dependence, and educational level for APPAGALO participants, in an intention-to-treat analysis.

	INTERVENTION	CONTROL	RR (95% CI)	*P* VALUE
By age group				
18-29 years old	(n = 56)	(n = 63)		
No smoking in the past 7 days	12.5	3.2	3,94 (0,85-18,18)	.082
Continuous abstinence	17.9	0	—	***<0,001***
30-45 years old	(n = 99)	(n = 91)		
No smoking in past 7 days	8.1	3.3	2,45 (0,67-8,96)	.158
Continuous abstinence	9.1	3.3	2,76 (0,77-9,87)	.101
By Fagerstrom score				
<=5	(n = 123)	(n = 123)		
No smoking in the past 7 days	11.4	4.1	2,8 (1,04-7,54)	.032
Continuous abstinence	13.8	2.4	5,67 (1,7-18,85)	.001
>5	(n = 32)	(n = 31)		
No smoking in the past 7 days	3.1	0	—	.999
Continuous abstinence	6.3	0	—	.492
By educational level				
<=12 years	(n = 68)	(n = 53)		
No smoking in the past 7 days	8.8	7.5	1,17 (0,35-3,93)	.999
Continuous abstinence	10.3	1.9	5,46 (0,69-42,99)	.078
>12 years	(n = 84)	(n = 89)		
No smoking in the past 7 days	10.7	1.1	9,54 (1,23-73,66)	.008
Continuous abstinence	14.3	2.2	6,36 (1,47-27,56)	.004

P values were obtained using Pearson´s Chi-Squared tests.

APPAGALO is a pioneering study in Latin America, where the participants were young women, mostly from middle to low-income districts, which presents multidimensional poverty levels higher than the average for the Metropolitan Region and the country as a whole (23% vs 20% respectively and an average 20% in Chile),[28] in a country with a high prevalence of smoking (33.3%). This no doubt constituted an unfavorable scenario to obtain results of clinical effectiveness with a non-pharmacological intervention and dependent on mobile technologies that operate completely at a distance. Nonetheless, our App resulted effective at 6 weeks, and more importantly, at 6 months for continuous abstinence regardless of the download and installation difficulties due to the restrictions of the clinical study. These restrictions (inclusion and exclusion criteria, consent forms etc.) would not be an obstacle once the app is available for direct download from the online store. Additionally, the APPAGALO study constitutes a contribution given that the contents developed by the team of experts with the best available evidence to create the mobile application could be widely available so that health teams can use them in instances of training and face-to-face approach with smokers.

APPAGALO emerges as a strategy to support smoking cessation in a national setting where there is little development of tobacco treatment. Therefore, it can contribute to strengthening the weakest aspect of the implementation of the WHO MPOWER strategy in our country.[13]

This app presents the advantages of mHealth interventions[15] specifically its low cost, its great potential for scalability towards the population, and the possibility that women who want to quit have a strategy that works through their mobile phones, privately and which can be accessed from various places.

A notable aspect of the study is the fact that both the intervention and the follow-up were carried out completely at a distance. This is relevant in scenarios of overburdening of health services in rural and hard to reach localities, with low training of health professionals in strategies to support smoking cessation. Even before the COVID-19 pandemic, evidence supported telehealth and mHealth interventions as effective strategies for smoking cessation.[29]

Furthermore, the current COVID-19 pandemic has shown the critical importance of having online services and systems to monitor health conditions and provide health advice and treatments as a complement to in-person support. Numerous new developments and research of the importance of at a distance services have emerged in regard to physical and mental health and health-related behaviors starting within a couple of months after the outbreak.[30-33] Also, cancer prevention and early cancer diagnosis have been impacted negatively during this pandemic.[34] In the UK, it is estimated that more than 1200 extra deaths due to a year delay in lung cancer diagnosis.[35] Importantly, after over two years since the beginning of the pandemic, telehealth and mHealth interventions, along with community prevention strategies, have become not only accepted but, in some cases, a recommended mode of health care delivery.[36] However, mobile cancer prevention interventions are scarce, and this App adds important information to knowledge and practice in this regard.

The design of APPAGALO considered an initial qualitative phase, so the result is an app whose content and language are culturally appropriate for the target population. This way of conducting research based on the participation of potential users and the community in general aims to incorporate their vision early in the design of the intervention, which contributes to its acceptance, its dissemination in the community, and therefore, to its public health potential.[37]

The experience developed in this study can serve as input for both the design and the monitoring of strategies that use mobile technologies in Latin America and beyond. Also, it can help to develop tools to support smoking cessation in other groups not included in this study, such as smokers in the general population, adolescents, and pregnant women.

Limitations

The main limitations of our study were the small sample size and incomplete follow-up.

Given the sample size and the results obtained, we calculated the study power for the primary outcome under ITT. For punctual abstinence, the power was 64.2% and for continuous abstinence, the power was 94.8%. Even with a smaller than anticipated sample size, the power for continuous abstinence is high.

The team went through great lengths to contact the women to complete the follow-up surveys, including telephone calls and WhatsApp messages from 20 student recruiters and advertising an incentive for those women that completed the study. However, as our loss to follow-up rates increased with time and are considerably high, we cannot rule out attrition bias. Nevertheless, the results of this study were subjected to the requirements of the intention-to-treat analysis, and positive outcomes regarding continuous abstinence with ITT analysis allow us to conclude that the app resulted effectively in increasing smoking cessation at 6 weeks and 6 months, even when the worst-case scenario was assumed, that is, that all participants without follow-up information continued to smoke.

Even though self-report has been widely accepted as a valid measure of abstinence,[17] it can be subjected to a memory bias. In this case, our primary outcome was measured at 6 weeks, which made this bias unlikely.

Although follow-up was incomplete, the follow-up efforts were carried out under a similar protocol for both arms of the study. Unfortunately, we were not able to contact nor offer any other help to the women who did not answer the follow-up calls. However, the literature supports that even attempting to quit (versus not making an attempt) is a valuable outcome in the lifetime of a smoker[27] and this was demonstrated during the time of follow-up in our study.

As with all digital interventions, there is a digital literacy gap reported specifically related to gender and older age groups in other international studies.[38,39] Nevertheless, a double format, including mHealth and some face to face interactions could solve this problem.[31]

As in any mHealth strategy dependent on an online connection, one important limitation is the access and quality of broadband or wi-fi to use the app. The access to the Internet on their mobile phones was a variable asked during the qualitative phase, but the quality of the signal and technical aspects of its performance were not measured during the follow-up.

APPAGALO can only be used by people who have Android-type phones. It should be mentioned that the possibility of developing the app for iPhone-type phones was evaluated and discarded due to the financial constraints of the study and given the massive use of Android phones in middle and low-income populations in Chile.

Conclusions

APPAGALO is an effective and safe strategy that can contribute to improving tobacco cessation in women. Its greatest potential lies in that it is simple, safe and could be easily scalable to wider populations.

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5. The media designer that gave Appagalo it's beautiful appearance: Gabriela Riveros.

Authors Contributions

JMG: Co-investigator in the grant leading to this research (Chief Investigator B) Contributed and involved in all phases of the trial. From conceptualization and design of the intervention to training of recruiters and communicating results to relevant stakeholders. She was principal contributor to all drafts of the manuscript.

AD: Statistician of the team. Carried out the statistical analysis of the research. She reviewed all drafts and contributed to the writing of the manuscript. She reviewed and approved its final draft.

CL: Project manager of the research; she carried out the qualitative phase that shaped the intervention and developed recruiters' materials and database as well as participating in all other phases of the research: design, implementation, and data collection. She reviewed and contributed to first and final drafts of the manuscript. She approved its final version.

JA: Recruitment manager of the team; he led and helped the 20 student recruiters of the team troubleshoot any complications throughout recruitment and follow-up of participants as well as participating in all other phases of the research: design, implementation, and data collection. He reviewed and edited first and final drafts of the manuscript. He approved its final version.

CA: In charge of clinical content of the intervention as well as participating in all other phases of the research: design, implementation, and data collection. She reviewed and edited first and final drafts of the manuscript.

MR: Community and primary care liaison for the study. She advised and facilitated recruitment and communications. She reviewed and edited first and final drafts of the manuscript. She approved its final version.

LV: Tobacco cessation expert. He advised on the clinical content of the intervention. He reviewed and edited first and final drafts of the manuscript. He approved its final version.

CB: Lead investigator in this research's grant. (Chief Investigator A). She secured funds and led all phases of the research. She contributed to and reviewed all drafts of the manuscript and approved its final version.

The contents of this article have not been previously presented elsewhere

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Figure A1. Branding images.

Appendix Description of the Intervention App

FROM ENROLLMENT TO D-DAY	WEEKS 1 TO 4 FROM D-DAY	WEEKS 5 TO 24 FROM D-DAY	ADDITIONAL TOOLS DURING THE STUDY
Four messages per day	Four messages per day	Three messages per week	Money saving calculator
Goal: To prepare women for quitting smoking	Goal: To support women during the first period after quitting smoking	Goal: To support women during the follow-up	Help button in case of nicotine cravings & help button in case of early relapse
Sample messages:	Sample messages:	Sample messages:	Sample message for cravings:
1. Capture motivation in an image (upload or take a picture)	*1. Distract yourself and keep busy*	*1. Stress relief exercises*	*Cravings are normal and last less than 10 minutes. Distract yourself and the craving will soon be over*
2. Think about the pros and cons of quitting smoking	*2. Choose a D-day and prepare context to quit smoking*	*2. Increase physical activity*	Sample message for early relapse:
3. Practice breathing exercise	*3. Recognize withdrawal symptoms and how to deal with them*	*3. Give yourself a gift for having quit smoking*	*Lapses are normal in the quitting process. Get back to your track of non-smoker and keep going!*
	Outcome measures:	Outcome measures:	
	App sent a question every night about whether they had smoked or not + telephone follow-up at week 4 from D-day	Telephone follow-up at 3 and 6 months	

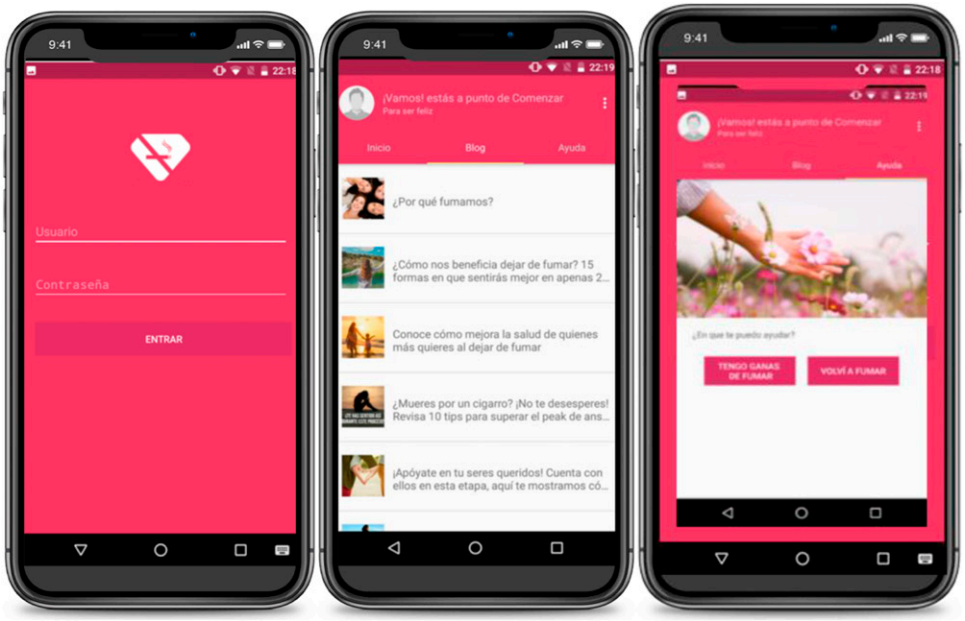

Figure A2. Smartphone images.

Table A1. Reasons for non-eligibility for the APPAGALO study. N = 156.

REASONS FOR INELIGIBILITY	%
Inclusion criteria	
Age out of study range	9.6
Smoking habit out of study range (at least 1 cigarette per day or 7 per week)	14.7
Does not want to quit within the next month	1.3
Does not own or use Android phone	27.6
Does not live in the catchment area or will move in the next year	10.3
Exclusion criteria	
Inability to answer telephone survey or sign an informed consent	0.0
Positive screening for risky alcohol consumption (AUDIT-C >3)	42.9

The percentages do not add up to 100, because each woman could present more than 1 reason for non-eligibility.

Table A2. Reasons for withdrawal from the study.

	INTERVENTION (N = 16)	CONTROL (N = 12)
App is not helping abstinence	5	3
App does not work well	1	3
App was uninstalled	1	1
Others (pregnancy, not willing to quit anymore)	9	5

Table A3. Actual-cases clinical effectiveness outcomes of the APPAGALO study.

	INTERVENTION	CONTROL	RR (95% CI)	*P* VALUE
Six weeks	(n = 80)	(n = 101)		
No smoking in past 7 days	18.8	5.0	3.79 (1.44-9.98)	.003
Continuous abstinence	24.1	3.0	8.10 (2.48-26.39)	<.001
Three months	(n = 70)	(n = 80)		
No smoking in past 7 days	17.1	18.8	.91 (1.82-.46)	.798
Continuous abstinence	15.7	15.2	1.03 (.49-2.19)	.930
Six months	(n = 28)	(n = 32)		
No smoking in past 7 days	28.6	6.5	4.43 (1.03-19.1)	.036
Continuous abstinence	28.6	6.3	4.57 (1.06-19.7)	.035

P values were obtained using Pearson´s Chi-Squared tests.

Table A4. Description of the behavior of women ending the study after 6 months using the Appagalo app.

	INTERVENTION (N = 28)	CONTROL (N = 32)	TOTAL (N = 60)	*P* VALUE
Previous attempts to quit smoking				
None	21.4	56.3	40.0	.006
At least 1	78.6	43.8	60.0	
Use of other smoking devices to quit smoking				
None	96.4	90.6	93.3	.616
Any	3.6	9.4	6.7	
Mean number of cigarettes smoked per day among participants still smoking at 6 months				
None	28.6	6.5	16.9	.008
1 or 2	25	16.1	20.3	
3 to 5	10.7	12.9	11.9	
More than 5	35.7	64.5	50.8	
Involvement in any vehicle crush since taking part of the study				
No	100	100	100	—
Yes	0	0	0	
Thumb injuries related to texting since taking part in the study				
No	100	100	100	—
Yes	0	0	0	

P values were obtained using Pearson´s Chi-Squared tests.