## **Research Article**

## Achieving smoking cessation through collaborative efforts between community pharmacists and health volunteers

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#### ABSTRACT

The objective of this study was to develop, implement, and evaluate a collaborative smoking cessation program (CSCP) involving community pharmacists and village health volunteers (VHVs) in a rural community. Our strategy included establishment, implementation, and reflection. The CSCP was established through group discussions among community pharmacists, VHVs, and a local officer. VHVs identified smokers and provided basic counselling, while community pharmacists provided smokers specific and intensive counselling. We also assessed clinical outcomes, such as peak expiratory flow rate (PEFR), exhaled partial carbon monoxide (PCO), and continuous abstinence rate (CAR). Finally, interviews from the reflection phase were conducted to investigate attitudes towards participating in the CSCP and unsuccessful quitting. CSCP was completed by 101 out of 108 initial participants. All were men, with an average age of  $55.2\pm10.75$  years. After six months, the CSCP resulted in a significant decrease in the mean PCO (*P*=0.010). Moreover, 23 smokers successfully quit smoking, yielding a sixmonth CAR of 22.8% and stated that the CSCP enforced their perseverance. However, 78 volunteers (72.2%) could not quit smoking owing to withdrawal symptoms and influence from their immediate environment. CSCP is a novel smoking cessation model, which should be promoted to enforce smoking cessation in the community. However, significant efforts and coordination of relevant stakeholders are required.

#### **Keywords**:

Community pharmacists, Village health volunteers, Smoking cessation, Collaborative smoking cessation program

## **1. INTRODUCTION**

Smoking, a modifiable lifestyle and a risk factor for several diseases, including cancer, cardiovascular disease, and respiratory disease, incurs a significant<sup>1</sup> burden on public health. By 2030, over eight million people worldwide are predicted to die from smoking-related conditions<sup>2</sup>. Approaches toward smoking cessation can either be pharmacological or non-pharmacological. The nonpharmacological approach includes brief intervention, health-professional counseling, and social support, which are particularly interesting<sup>3</sup>. Smoking cessation health policy is one of the most challenging tasks, as evidenced by poor cessation rates (14.6-27.6%)<sup>4</sup>. Intervention for smoking cessation also needs the participation of the community; such intervention is, however, limited<sup>5</sup>. Although pharmacists are an important component of health care providers in smoking cessation strategies, they mainly constitute an office-based service<sup>6</sup>. A previous smoking cessation program involving collaboration between village health volunteers (VHVs) and community pharmacists produced a satisfactory abstinence rate six months after the program (26%); the Umnuaypornlert study evaluates only the effectiveness of community health workers (CHWs) in a smoking cessation program. However, this study only evaluates the effectiveness of community health workers (CHWs) in a smoking cessation program. Furthermore, the assessment of CHWs' knowledge was not ensured before providing the program, the sample size of the study was relatively small, and the program details were vague<sup>7</sup>.

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Community pharmacy services in Thailand, especially those for non-communicable diseases (NCDs) screening, such as hypertension, diabetes, and cardiovascular diseases, all involving smoking habits<sup>8-9</sup>, have recently expanded considerably. The Thai Pharmacy Network for Tobacco Control (TPNTC), a non-governmental organization established in 2004, has been promoting smoking cessation in community pharmacies<sup>10</sup>. Since the year 2018, Thailand has established standard smoking cessation guidelines, elaborating the crucial roles of community pharmacists in counseling, identifying failure, and dispensing (with monitoring) medication (such as nicotine and varenicline) in smoking cessation programs<sup>10</sup>. Lertsinudom's study has demonstrated the effectiveness in service with high success rates<sup>9</sup>, consistent with those from the UK study<sup>11</sup>. However, this service is delivered through a pharmacy-based setting, which requires the patient to walk into the service<sup>11</sup>. This approach may limit access for smokers who are less interested in quitting. Since the establishment of the guideline, community pharmacies have proven to be pivotal to the success of smoking cessation services<sup>9</sup>. In 2020, the universal coverage (UC) program strategically incorporated community pharmacies with smoking cessation services, thereby improving their conveniences, effectiveness, and approach<sup>9</sup>. As a result, the importance and quality of smoking cessation services are highlighted, necessitating time and effort to program visits and explore documents with consistent counseling and monitoring. Gaps in knowledge and understanding of the roles of community pharmacists and others are primarily responsible for the low smoking cessation rates and relapses<sup>12</sup>.

Multiple, repetitive, and continual interventions, including those from counselors, family members, and surrounding people, improve smoking cessation rates through changes in attitudes, behaviors, and perseverance<sup>13</sup>. Smokers who do not live in the same community as their counselors may not receive as frequent interventions as necessary. The introduction of community healthcare providers (village health volunteers; VHVs) who have close contact with smokers contributes to the smoking cessation program as a whole. VHVs are regarded as a key social asset for Thailand's primary health care. Their roles are mainly to assist in promoting and preventing health and diseases in the community. VHVs are commonly well-known and respectful. They are willing to dedicate themselves to their community. To become a VHV, a person must be selected by community members and must pass the training program accredited by the Ministry of Health<sup>14</sup>. Based on these qualifications, VHVs are seen as key motivators for smoking cessation. To establish collaborative programs between VHVs and community pharmacists, considerable efforts from various collaborators are needed through multiple meetings and social interactions among the key personnel from all parties, including VHVs, community pharmacists, local

officers of primary health care (so-called local officers), and community leaders, which will lead to the design and establishment of a cooperative cessation program for implementation in that particular community.

At this early stage, efforts to harmonize community pharmacists and VHVs in smoking cessation services are essential as they form a collaborative team. In this study, we developed, implemented, and evaluated a pharmacist-VHV collaborative smoking cessation program that improved clinical outcomes, including peak expiratory flow rate (PEFR), exhaled partial carbon monoxide (PCO), and continuous abstinence rate (CAR). Furthermore, clinical outcomes were compared between pre- and postintervention. The findings of this study will demonstrate a new model of a community-involved smoking cessation program.

#### 2. MATERIALS AND METHODS

#### 2.1. Study Design

This study utilized an action research design.

#### 2.2. Settings

The study was conducted in the Don Chang subdistrict of Khon Kaen, Thailand in 2020. The sub-district consisted of eight villages covering an area of  $43.6 \text{ km}^2$ , with a population of 5,031 people residing in 1,106 households<sup>15</sup>.

#### 2.3. Participants

#### 2.3.1. Development and Implementation of the Program

Community pharmacists from CPS-KKU (n=4), VHVs (n=105) and a local officer (n=1) were involved in the development and implementation of the program.

#### 2.3.2. Smokers

Inclusion criteria: Adult current smokers (age >18 years) who expressed willingness to quit smoking at a preparation level based on the Trans-Theoretical model. Exclusion criteria: Individuals who were unable to speak, read, or understand the Thai language and those with severe mental illness.

Recruitment process: Village Health Volunteers (VHVs) informed potential participants about the study and scheduled appointments for analysis with smokers who wished to quit smoking. A total of 146 smokers were assessed for eligibility, and 108 were ultimately recruited. (Figure 1) Smokers were classified in two groups: light and heavy. A light smoker is defined as a smoker who reports consuming less than 10 cigarettes per day or smoked the first cigarette more 5 min after waking up.

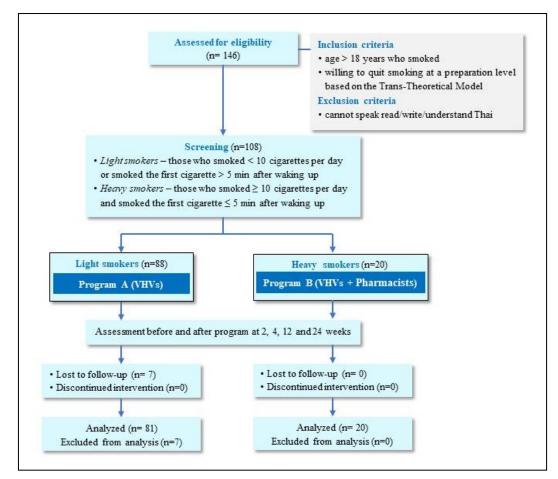


Figure 1. Flow diagram for the implementation of collaborative smoking cessation program (CSCP).

Activity	Method	Team members	Output
Review case studies and update the current situation within the community	Participatory group discussion (1st)	local officers (n=3), VHVs (n=105), pharmacists (n=4)	Strategies for successful smoking cessation
Design the collaborative smoking cessation program	Draft the program to fit with the relevant guidelines	pharmacist (n=3)	A draft of the collaborative smoking cessation program
Review the draft of the collaborative smoking cessation program	Participatory group discussion (2nd)	Local officer (n=1), representative VHVs (n=9), pharmacists (n=1)	A revised protocol for collaborative smoking cessation
Agreement among team members	Participatory group discussion (3rd)	Local officer (n=1), VHVs (n=90), pharmacists (n=4)	Establishment of the collaborative smoking cessation program (CSP)
Work plan	Participatory group discussion (4th)	Local officer (n=1), VHVs (n=90), pharmacists (n=4)	Data collection methods and forms related to the outcomes
Training and assessments of	Workshop training	VHVs (n=92) pharmacist (n=9) local officer (n=1)	Trained team members for the collaborative smoking cessation program

A heavy smoker is defined as a smoker who reports consuming 10 cigarettes or more per day and the first cigarette less than or equal to 5 minutes after waking up.

#### 2.4. Program

#### 2.4.1. Program Development

The Collaborative Smoking Cessation Program (CSCP) was developed through brainstorming meetings

involving community pharmacists, VHVs, and a local officer responsible for primary health care. Program components and interventions were established based on the inputs and objectives of the stakeholders (Table 1).

#### 2.4.2. Program Implementation

The CSCP was implemented voluntarily by VHVs, with data collection conducted from January to June 2020. VHVs and local officers participated in a pharmacist-led workshop to be trained as tobacco cessation providers. VHVs who completed the workshop activities and passed the assessment were qualified to implement the program. The program was facilitated by the local officer and mentored by pharmacists. Specific dates and visits were scheduled for follow-up and encouragement of the smokers.

#### 2.5. Outcomes

The program outcomes assessed included Peak Expiratory Flow Rate (PEFR), Partial Carbon Monoxide (PCO), attitudes towards participating in the CSCP and Continuous Abstinence Rate (CAR). The CAR was determined through monitored PCO in conjunction with details from the interviews coordinated by the VHVs at four consecutive visits. The smokers with PCO of <10 ppm and no cigarette smoking recorded in the interview data were considered as CAR, as these data indicated smoking cessation throughout the study period. CAR was measured six months after the intervention.

#### 2.6. Data Collection

#### 2.6.1. Sociodemographic Data

Sociodemographic information such as age, income, smoking behavior, and Fagerström score was collected by VHVs.

#### 2.6.2. Outcome Data

PEFR and PCO measurements were taken at baseline, weeks 2, 4, 12, and 24 to assess changes in respiratory function and carbon monoxide levels by VHVs.

#### 2.6.3. Semi-Structured Questionnaire

A semi-structured questionnaire was used to collect information on withdrawal symptoms, obstacles, and problems related to smoking cessation. The questionnaire consisted of multiple parts and was administered through face-to-face interviews with the participants. Finally, interviews from the reflection phase were explored to investigate attitudes towards participating in the CSCP and unsuccessful quitting. The questionnaire was administered to smokers who were unsuccessful in quitting smoking. Seventy-eight smokers participated in this survey conducted by VHVs. The question composed of a checklist of reasons for failure.

#### 2.7. Data Analysis

The Sociodemographic data collected were analyzed using descriptive statistics (means and standard deviation (SD) or percentages) where applicable. For outcomes that were compared pre- and post-intervention were PEFR and PCO, which the Wilcoxon Signed-Ranks test were used to analyze the data. The chi-square test was used for

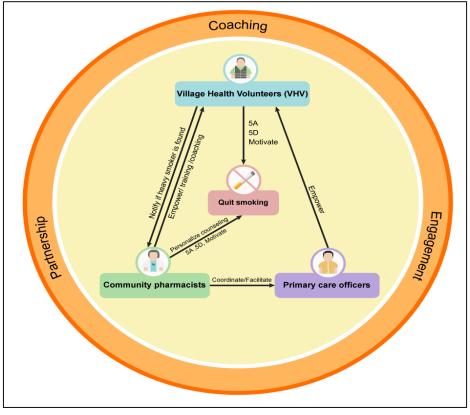


Figure 2. Collaborative smoking cessation program.

Note: (5A: ask, advise, assess, assist, and arrange; 5D: delay, distract, drink water, deep breathing, and discuss).

analyzing categorical variables. Significance levels were set at 0.05. The authors determined significant improvement or decline in PEFR and PCO by comparing the measurements at different time points (baseline and week 24) using appropriate statistical tests. Data were managed and analyzed using the Stata Version 14 software (StataCorp, Texas, USA, Serial number: 401506248924)

### **3. RESULTS**

# **3.1.** Establishment of the collaborative smoking cessation program

The planning step resulting in establishing the CSCP was ensured by all parties involving health care providers within the community, coordinated by one local officer, 105 VHVs, and four CPS-KKUs (Figure 2).

The VHVs recruited and counseled all smokers who consented to enroll in the program. Moreover, heavy smokers were additionally motivated by the CPS-KKU.

#### 3.1.1. Characteristics of participating smokers

In this study, only 101 of the 108 eligible volunteers completed the program. All of them were men (age  $55.2\pm10.75$  years old), the majority of whom had received

Table 2. Baseline characteristics of volunteers.

primary education (63.9%), were married (84.3%), had a monthly income of <10,000 Baht (65.7%), working (61.1%), and had no underlying disease (63.0%) (Table 2).

#### 3.1.2. Smoking-related behaviors

We noted that 61.50% of the volunteers occasionally drank alcoholic beverages, 38.95% had a tobacco index of a minimum of 15 pack-years, and over half (57.41%) smoked  $\geq$  10 cigarettes per day. The Fagerström test was used to measure nicotine dependence levels<sup>16</sup>. Most volunteers (54.6%) had scores between 4-6, indicating moderate nicotine addiction. Moreover, over half of the recruited cases (68.52%) smoked after meals, whereas approximately three-quarters (75.61%) smoked during breaks at the workplace (Table 3).

### 3.1.3. Clinical outcomes

Table 4 shows the comparison of clinical outcomes between pre- and post-intervention. The teamwork led to significant decrease in mean PCO six months after intervention (P=0.010). Moreover, no significant decrease was observed in the heart rate (HR) and body weight (P=0.027 and 0.011, respectively).

Table 5 depicts the number of volunteers initially

Items	n	%
age (year)(mean ± SD)	55.23±10.75	
Age		
<u>≤40</u>	10	9.3
41-50	21	19.4
51-60	45	41.7
61-70	25	23.6
≥71	7	6.5
Education		
Primary	69	63.9
secondary school	25	23.2
high school	10	9.3
Diploma	2	1.9
Bachelor	2	1.9
Marital status		
single	12	11.1
married	91	84.3
widowed	3	2.8
divorced	2	1.9
Occupation		
labor	66	61.1
government officer	2	1.9
state enterprise	3	2.8
business	4	3.7
private employee	4	3.7
student	1	0.9
not available	28	25.9
Income (Baht/month)		
none	7	6.9
<10,000	71	65.7
10,000-20,000	20	18.5
20,001-30,000	7	6.5
>30.000	3	2.8

Table 3. Smoking-related behaviors at the initial point.

Variable	n	%
Alcohol drinking (n=96)		
No	21	21.9
Yes	65	78.1
In the past (stopped)	9	9.3
Sometimes	59	61.5
Daily	7	7.2
Pack-year* (n=95) (cigarettes/day-year)		
<1.0	7	7.4
1.0-4.99	25	26.3
5.0-14.99	26	27.4
≥15	37	38.9
Smoked cigarettes per day (Average 10.2±6.7)		
<10	46	42.6
≥10	62	57.4
Fagerström score		
Low (<4)	40	37.1
Moderate (4-6)	59	54.6
High (7-10)	9	8.3
Smoker types		
Social dependence (n=105)		
smoke after meals	74	70.5
smoke with or after drinking coffee	15	14.3
smoke with alcoholic drinks	16	15.2
Psychological dependence (n=98)		
smoke during a work break	62	63.3
smoke during work	19	19.4
smoke when stress	17	17.3

Table 4. Comparison of clinical outcomes at initial and week 24 after enrollment.

	At initial	Week 24
PEFR (%) (n=106)	89.6 (79.4, 97.51)	89.0 (74.2, 98.3)
PCO (ppm) (n=101)	11 (7, 13)	8* (4, 11)
Vital signs		
Systolic (mmHg) (n=92)	125 (125, 131)	126 (120, 130)
Diastolic (mmHg) (n=92)	80 (74, 81)	79 (74, 84)
Heart rate (bpm) (n=92)	79 (76, 81)	69.5* (75, 85)
Body weight (kg) (n=108)	61.9 (55, 67.5)	60.8* (54, 65)

Note: \*p<0.05 by Wilcoxon signed rank test; variables are described as medians with interquartile ranges in brackets

**Table 5.** Number of volunteers with interview data grouping as number of smoked cigarettes and results from measured exhaled CO (PCO) during the initial week and week 24 after enrollment for continuous abstinence rates.

	Initial (n=108)	Week 24 (n=101) %
Changes in the number of cigarettes smoked#	108 (100.0%)	78 (77.2%)
Decreases		31
Increases		11
No change		36
Smoking cessation		23 (22.8%)
PCO <10 ppm	40 (37.0%)	59 (58.4%)*
PCO ≥10 ppm	68 (63.0%)	42 (41.6%)

Note: #shown as the no. of volunteers with changes in the no. of cigarettes smoked at visit 4 from those at initial; \* p < 0.001, \*\* p < 0.05

 Table 6. Number of volunteers with improved PEFR between successful and unsuccessful quitters.

Δ PEFR <sup>a</sup>	<b>Smoking (N= 101)</b>		P value
	Success (n=23)	Failure (n=78)	_
Non-improved <sup>b</sup>	10 (43.48%)	52 (66.67%)	0.045
Improved <sup>c</sup>	13 (56.52%)	28 (33.33%)	

Note: <sup>a</sup> $\Delta$  PEFR= post PEFR-prePEFR, <sup>b</sup> non-improved refers to  $\Delta$  PEFR  $\leq$  0, <sup>c</sup> improved refers to  $\Delta$  PEFR > 0. Statistical analysis was tested by Chi-squared test.

and after visits, involving semi-structured interviewing by VHVs in conjunction with PCO measured by pharmacists. We noted that 23 voluntarily quit smoking (22.8%) and achieved a CAR from visits 1 through 4. They constituted 58.4% of volunteers with PCO <10 ppm. After visit 4, volunteers with PCO of  $\geq 10$  ppm decreased from 63.0% to 41.6%, (Table 5) indicating a potential reduction in smoking behavior in line with the data obtained from the interview (31 volunteers attempted to decrease smoking). Although these volunteers were not successful, this change of behavior could be attributed to CSCP. The proportion of volunteers with PCO <10 ppm significantly increased from 37.0% to 58.4% (P<0.05), revealing the effect of CSCP (Table 5). The number of volunteers with improved PEFR amongst quitters (56.52%) was significantly higher than that observed in those who were unsuccessful in quitting (33.33%) (Table 6).

At the interviews, all volunteers who quit smoking (n=11) stated that the four visits to the CSCP with the same VHVs reminded them to persevere. They expressed their confidence in the CSCP and the service of all team members, particularly the collaborative efforts. However, 78 volunteers (72.2%) could not cease smoking even after the program for various reasons: 75% of them had with-drawal symptoms, and 33.33% were influenced by their immediate environment (Figure 2).

#### 4. DISCUSSION

Successful smoking cessation normally requires multiple, repetitive, and continual interventions. Our findings confirmed that pharmacist collaboration with VHVs significantly improved smoking cessation in the community. Moreover, the effects of smoking cessation programs in the community were assessed through clinical outcomes. The CAR at six months was satisfied by 22.8%. This is in line with a previous study by Tongsri et al. (2021), demonstrating that counseling programs by community pharmacists encouraged smokers to quit smoking in a satisfactory manner<sup>17</sup>.

We observed a significant difference in the CAR at six months after the intervention; however, there was no significant difference among other related outcomes. This could be explained by the fact that pharmacists collaborated with VHVs, who majorly identified individuals and provided support to quit smoking. We also observed that VHVs could promote health literacy and self-efficacy in assisting volunteers with smoking cessation, thereby encouraging them to stop smoking<sup>18</sup>. Moreover, our findings were consistent with those of Choosakul et al. (2022), demonstrating that VHV-based intervention for smoking cessation slightly increased the cessation rate<sup>19</sup>. Although the PEFR did not change significantly between pre- and post-intervention, the number of volunteers with improved PEFRs was higher among individuals who quit smoking. Moreover, the PCO was

also significantly improved. These findings suggest that CSCP positively enhanced smoking cessation in the community. This leads to improved lung function and health.

Our findings revealed that body weight decreased significantly after the program, which is in contrast to previous evidence. Theoretically, successful quitters typically gain body weight. This could be attributed to increased appetite and reduced energy expenditure<sup>20</sup>. However, Jitnarin (2014) reported that light smokers have lower body mass index than moderate and heavy smokers in Thailand<sup>21</sup>. Based on this study, we believe that our volunteers tended to smoke less after program completion and became light smokers, thereby explaining the significant reduction in body weight. Evidence on the effect of smoking cessation on HR is limited. In this study, heart rate reduced significantly after program completion. West and Schneider previously reported that HR drops from 74 to 65 beats per minute after one day of smoking cessation<sup>22</sup>. The reduced HR may be attributed to reduced nicotine levels in those who quit smoking<sup>23</sup>.

The community pharmacists are vital in implementing smoking cessation. Meta-analysis results suggested that pharmacist interventions significantly increased the short- and long-term abstinence rate compared to the control<sup>24</sup>. Brett et al. (2019) demonstrated a significantly higher likelihood of smoking abstinence for pharmacistled intervention compared to that with the standard or usual care<sup>11</sup>. Additionally, pharmacist-led intervention for smoking cessation was found to be beneficial compared to no intervention. Behavioral support and nicotine replacement therapy provided by pharmacists are both effective and cost-effective in smoking cessation<sup>25</sup>. However, although these interventions are known to be effective in smoking cessation, they have not been widely adopted<sup>25-26</sup>. Some barriers may influence unsuccessful smoking cessation. For example, very few pharmacies in Thailand have documented and kept profiles of smokers<sup>12</sup>.

Community pharmacists collaborating with VHVs are vital in achieving smoking cessation in the community. To the best of our knowledge, this is the first study demonstrating the effect of collaborative efforts between community pharmacists and VHVs in enhancing smoking cessation. In this study, community pharmacists trained the VHVs to provide basic advice and perform lung function tests for monitoring. This collaborative program offered an opportunity for smokers who had never attempted to quit smoking to consider quitting, similar to findings from a previous study that emphasized on enhancing knowledge and positive attitudes of VHVs regarding smoking cessation. However, the latter study employed a strategy that reduced the number of cigarettes smoked per day (from 7.03 to 5.72), though the reduction was not significant. Prior studies did not categorize smoking addiction severity and cessation counseling as a group intervention. Conversely, the current study delivers tailored counseling to individual participants based on their addiction level, rendering it more individualized and potentially leading to a higher cessation rate.

Moreover, they neither trained VHVs to perform lung function tests for monitoring nor measured smokingrelated outcomes, making the program inefficient and unreliable<sup>27</sup>. Additionally, our findings outperformed the six-month cessation rate of 22.8% observed in a study by Umnuaypornlert (2021) (26.0%)<sup>7</sup>. This confirms that community health workers can provide individually tailored solutions when trained intensively.

If our model is implemented, it has the potential to reduce the number of smokers visiting healthcare settings and community pharmacies. This would enable healthcare professionals to focus on more severe patients. Simultaneously, the community will experience an increased smoking cessation rate and a reduced second-hand smoking rate. Moreover, this strategy raises the community's awareness of the hazards of smoking.

This study did not involve other civil society stakeholders (social welfare, NGOs, or local politicians) in the program. By involving these parties, the collaborative efforts to achieve smoking cessation can be multiplied.

Generalization can be implemented if the team establishes a cooperative program for use. The collaborative smoking cessation program developed in this study is not specific to Thailand and could be implemented in other developing countries (e.g. Vietnam, Malaysia, Iran and China) with similar healthcare settings<sup>28-30</sup>. In many countries, community pharmacists and community health workers/volunteers play important roles in healthcare delivery, including promoting healthy behaviors such as smoking cessation. However, some modifications may be necessary to adapt the program to the specific contexts of different countries. For example, the training of VHVs may need to be modified to meet local regulations and guidelines.

Although this study was performed through solid teamwork, some limitations still exist. Our study was developed based on a specific context in a particular setting<sup>31</sup>. Our study recruited men only, which corresponds to the natural figure of Thailand, where more men tend to smoke compared to women<sup>21</sup>. Moreover, there was room for selection bias for two reasons. First, our volunteers were invited by VHVs and agreed to join the program, which could have been influenced by personal connections. Second, we recruited only volunteers willing to quit smoking, enhancing the cessation rate more than that of the general population. Furthermore, our study demonstrates only a short-term benefit for smoking cessation. Therefore, we recommend studies that monitor smokers for a minimum of one year to assess relapse rates.

#### **5. CONCLUSION**

CSCP involving community pharmacists and VHVs is an innovative model for smoking cessation, which can be developed and established directly in the community. This study demonstrated that implementation of such a model can result in acceptable smoking quit rate. Therefore, this collaborative program should be promoted to enforce smoking cessation in the community. However, to successfully implement it, great efforts and continuous coordination are required from the local community, government, and non-government stakeholders.

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#### **Conflict of interest**

None to declare.

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#### **Ethics approval**

This study was approved by the Khon Kaen University Ethics Committee in Human Research, according to the Declaration of Helsinki and Good Clinical Practice guidelines (ICH GCP) No. HE622068, dated 17 July 2019.

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#### **Author contribution**

Conceptualization, PP., AT., SA., and SL.; methodology: PP. and SL.; formal analysis: PP.; investigation: PP.; resources: PP.; data curation: PP.; writing—original draft preparation, PP.; writing – review and editing: PP., AT., SA., and SL.; supervision: PP., AT., SA., and SL.; project administration: PP.; validation: PP.; funding acquisition: PP. and SL. All authors have read and agreed to the published version of the manuscript.

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