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PI: Shelley, Donna R	Title: Implementing tobacco use treatment guidelines in community health centers in Viet	
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ABSTRACT

Vietnam has a smoking prevalence that is the second highest among South East Asian countries (SEACs). With a population of approximately 90 million, Vietnam also has the second largest total number of adult smokers (over 16 million) in SEA. According to the World Health Organization (WHO), most reductions in mortality from tobacco use in the near future will be achieved through helping current users quit. Tobacco use treatment, as defined by the U.S. Preventive Health Service Guideline (Guideline) on *Treating Tobacco use and Dependence*, is evidence-based and highly cost-effective. Yet, in the U.S. and globally, adoption of recommended care is suboptimal. The objective of this proposal is to fill the current research-to-practice gap by conducting a randomized controlled trial that compares the effectiveness and cost effectiveness of two practical and highly replicable strategies for implementing evidence-based guidelines for the treatment of tobacco use in public health clinics in Vietnam. The proposed implementation strategies draw on evidence-based approaches, and the WHO's recently released guidelines for implementing Article 14 of the Framework Convention on Tobacco Control (FCTC). The FCTC is an evidence-based treaty that was developed by the WHO in response to the globalization of the tobacco epidemic. Vietnam ratified the FCTC in 2004; however, they have not taken steps to implement Article 14 which specifies the need to integrate best practices for treating tobacco use and dependence into routine preventive care. The proposed implementation strategies also build on the growing literature that supports the effectiveness of integrating community health workers as members of the health care team to improve access to preventive services. We propose a two arm, cluster randomized controlled trial that will compare the effectiveness and cost effectiveness of two multi component strategies for implementing tobacco use treatment guidelines: 1) Technical assistance, training, plus clinical reminder system (TTC) vs. 2) TTC + referral to a community health worker (CHW). The primary outcome is provider adherence to tobacco use treatment guidelines (implementation effectiveness). The secondary outcome is six month biochemically verified smoking abstinence. We will conduct a formative evaluation prior to implementation to evaluate to assess current policies, systems of care and practice-level barriers and facilitators for tobacco use screening and treatment in public health clinics and inform modifications to the implementation strategies. Guided by an organizational model of innovation implementation, we will also examine organizational factors associated with effective implementation of provider adherence to tobacco use treatment guidelines. The study will be conducted in 26 public health clinics in two districts (rural and urban). The long-term goal of this research is to provide critical new knowledge to facilitate the widespread implementation, dissemination and sustained utilization of evidence-based tobacco use treatment strategies globally and in the U.S.

PROJECT NARRATIVE

Vietnam has a smoking prevalence that is the second highest among South East Asian countries (SEAC). Cost effective treatment for tobacco use exists, yet globally, adoption of recommended care into routine clinical practice in Vietnam and other SEACs is suboptimal. This study will test models of care that have promise to increase implementation and dissemination of evidence-based tobacco use treatment in health care systems in SEACs and the US

SPECIFIC AIMS

Almost half of adult men in Vietnam are current smokers, a smoking prevalence that is the second highest among South East Asian countries (SEACs). With a population of approximately 90 million, Vietnam also has the second largest total number of adult smokers (over 16 million) in SEA. According to the World Health Organization (WHO), most reductions in mortality from tobacco use in the near future will be achieved through helping current users quit. Tobacco use treatment, as defined by the U.S. Preventive Health Service Guideline (Guideline) on *Treating Tobacco use and Dependence*, is evidence-based and highly cost-effective. The Guideline, which is endorsed by the WHO, provides strong evidence that asking all patients about tobacco use, advising smokers to quit, assessing readiness, providing assistance (i.e., counseling) and arranging follow-up (the 5As) can significantly increase smoking abstinence rates. Yet, in the U.S. and globally, adoption of recommended care into routine clinical practice is suboptimal. This is in large part due to a lack of research on strategies for implementing evidence-based tobacco use treatment guidelines.

The long-term goal of the project is to develop a generalizable model for implementing evidence-based tobacco use treatment within existing health systems locally and globally. The objective of this proposal is to fill the current research-to-practice gap by conducting a randomized controlled trial that compares the effectiveness and cost of two practical and highly replicable strategies for implementing evidence-based guidelines for the treatment of tobacco use in public health clinics in Vietnam. The proposed implementation strategies draw on evidence-based approaches and the WHO's recently released guidelines for implementing Article 14 of the Framework Convention on Tobacco Control (FCTC). The FCTC is an evidence-based treaty that was developed by the WHO in response to the globalization of the tobacco epidemic. Article 14 specifies the need to integrate clinical best practices for treating tobacco use and dependence into routine preventive care. The proposed implementation strategies also build on the growing literature that supports the effectiveness of integrating community health workers as members of the health care team to improve access to preventive services.

Vietnam ratified the FCTC in 2004 and has since reached several milestones, primarily in the area of smoke free air and tax policies. But like other low middle-income countries (LMICs), they have not taken steps to implement Article 14. This research proposal will leverage a unique partnership of academic, public health and government investigators, including researchers at New York University, Johns Hopkins University, University of North Carolina, the Ministry of Health in Vietnam, the WHO, researchers from the Hanoi Medical University and the Vietnam Institute of Social Medical Sciences (ISMS). It builds on prior NIH funded research collaborations and on Dr. Nguyen's (Co-PI and Director, ISMS) extensive experience in conducting large-scale research and evaluation projects across all levels of the Vietnam health care delivery system, including implementing preventive service guidelines in public health clinics. The proposal also leverages local expertise and supports the objectives of the Vietnam National Action Plan for implementation of all components of the FCTC. The trial will be conducted in 26 public health clinics in two districts in Vietnam.

The specific aims are to:

- 1) **Conduct a formative evaluation** to assess the contextual factors of the intervention settings (i.e., district level policies and organizational level characteristics) that may influence tobacco use treatment in CHCs and to inform necessary modifications to the proposed implementation strategies.
- 2) **Compare the effectiveness and cost effectiveness of two multi-component strategies for implementing tobacco use treatment guidelines:**
 - a) Technical assistance, training, plus clinical reminder system (TTC) vs.
 - b) TTC + referral to a community health worker (CHW).

The primary outcome is provider adherence to tobacco use treatment guidelines (i.e., implementation effectiveness) and the secondary outcome is biochemically verified six month smoking abstinence.

- 3) **Use a mixed methods approach to explore potential theory driven mechanisms**, at the organizational level, hypothesized to explain the comparative effectiveness of the implementation strategies.

Guided by an organizational model of innovation implementation, our central hypothesis is that the addition of a referral system (the community health worker) will be superior to training, technical assistance and clinical reminders alone in increasing implementation effectiveness. The ultimate goal of the proposed research is to provide critical new knowledge to facilitate the widespread implementation, dissemination and sustained utilization of evidence-based tobacco use treatment strategies globally and locally.

B. SIGNIFICANCE

Smoking rates in Vietnam are one of the highest in the world.¹⁻³ If current smoking rates are not addressed it is estimated that in 10 years, tobacco use will be responsible for about 25% of adult male deaths in Vietnam.⁴ Encouragingly, two-thirds of current smokers in Vietnam are planning to or thinking about quitting and over half attempt to quit annually.¹

Most reductions in mortality from tobacco use in the near future will be achieved through helping current users quit.⁵⁻⁸ Tobacco use treatment, as defined by the U.S. Preventive Health Service Guideline (PHS Guideline) on *Treating Tobacco use and Dependence*, is evidence-based and highly cost-effective.⁸ The Guideline, which is endorsed by the World Health Organization (WHO), is based on a meta-analysis of over 8000 studies and provides strong evidence that asking all patients about tobacco use, advising smokers to quit, assessing readiness, providing assistance and arranging follow-up (the 5As) can significantly increase smoking abstinence rates.⁸ Yet, in the U.S. and globally, adoption of guideline recommended care into routine public health and clinical practice is suboptimal.⁸⁻¹⁰

Implementing evidence-based tobacco use treatment is a core provision in the WHO Framework Convention on Tobacco Control (FCTC). The FCTC is an evidence-based treaty that was developed by the WHO in response to the globalization of the tobacco epidemic.¹¹ These FCTC regulatory strategies include implementing evidence-based smoking cessation treatment in public health care delivery settings. Article 14 of the FCTC states that, “each country shall take effective measures to promote cessation and adequate treatment for tobacco dependence.”¹² In an effort to comply with Article 14, over 20 countries have developed guidelines for treating tobacco use which are based on the PHS Guideline.⁸ Although Vietnam has a strong public health delivery system, according to the 2010 Global Adult Tobacco Survey, like other South East Asian Countries (SEACs), services to treat tobacco dependence are not readily available to smokers.¹ Barriers to integrating treatment into routine primary care in low middle-income countries (LMICs) are similar to those in the U.S. and include: 1) inadequate training of health care providers, 2) lack of evidence-based systems for implementing guideline recommended care, and 3) a lack of research on strategies for implementing tobacco use treatment guidelines in LMICs.¹³

Closing the gap between research and practice is stymied by limited research on cost effective strategies for integrating cessation services into routine practice. Drawing upon a burgeoning implementation science literature,¹⁴⁻²³ and a growing literature that supports the effectiveness of integrating community health workers as members of the health care team to improve access to preventive services,²⁴⁻³¹ we propose to compare the effects of two organization-level strategies: 1) Technical assistance, training and a clinical reminder system (TTC) vs. 2) TTC + referral to community health workers (CHW) for additional counseling and support.

Technical assistance, training and clinical reminders. Technical assistance to reinforce training and assist with system changes, in many forms (e.g. academic detailing, practice facilitation), has been shown to be an important component of effective practice change.^{17,18,32} In addition, the PHS Guideline strongly recommends staff training and clinical reminder systems as the foundation for increasing adherence to guidelines recommended care.⁸ However, several studies have shown that adding a referral system can enhance rates of provider adherence to tobacco use treatment guidelines and increase smoking abstinence rates beyond that of training and clinical reminders alone.¹⁸⁻²³

Referral to CHW. The Ask, Advise Refer model may work by simplifying guideline adoption, providing the means and opportunity to delegate the follow-up and additional counseling recommended by the PHS Guideline.²³ The impact of referral systems on adherence to tobacco use treatment guidelines is also supported by a recent study in Malaysia.³³ This study, conducted in diabetes clinics, similarly found that providing a referral to stand alone cessation clinics motivated clinicians to routinely provide cessation advice. Therefore, offering a referral option for additional counseling may enhance quit attempts and cessation rates. However, the Malaysian model of creating stand-alone cessation clinics is too expensive to disseminate widely and stands in contrast to recommendations from the WHO’s recently published guidelines for implementing Article 14 which state: “In order to promote tobacco cessation and develop tobacco dependence treatment as rapidly as possible and at as low a cost as possible, countries should use existing resources and infrastructure.”¹² This proposal leverages existing infrastructure elements including a robust public health care delivery system with an extensive network of community health workers (CHWs).

In Vietnam, as in other LMICs, CHWs have a strong track record of effectively delivering preventive services and increasing the reach of these programs.^{24,26} As a critically important member of the public health care system, it is surprising that in LMICs there are no studies evaluating the role of CHWs as a referral resource for increasing access to evidence-based smoking cessation services, and we are aware of only one study in the

U.S.²⁵ Consistent with WHO Guidelines for implementing Article 14, CHWs offer a sustainable resource for ensuring wide access to support for tobacco users who wish to quit.

The proposed study has relevance to U.S. health care system. Studies in the U.S. have also shown that CHWs can facilitate access to care, improve the quality of service delivery and improve outcomes related to high priority health care issues like managing chronic illness.^{25,27-31} CHWs are recognized in the Patient Protection and Affordable Care Act as important members of the health care workforce and, in 2010, CHWs were recognized by the department of labor with their own Standard Occupational Category.³⁰ In the context of current efforts to restructure the delivery of primary care (e.g. patient centered medical home (PCMH)) Rosenthal et.al. noted that integrating CHWs into health teams operating in PCMHs is essential for success of this model.²⁷ In terms of specific relevance to tobacco use treatment, a recent Institute of Medicine report called for greater efforts to adopt strategies that facilitate implementation of effective tobacco cessation interventions in health care settings.³⁴ The current study has the potential to provide relevant information about what it takes to implement and sustain an integrated CHW model for disseminating and implementing evidence-based tobacco use services in community-based practices.

Vietnam is poised to develop replicable models of care delivery that address gaps in the reach and sustainability of evidence-based tobacco use treatment. The dearth of effective tobacco cessation services in Vietnam is not the result of a lack of commitment to tobacco control. The government ratified the FCTC in 2004, and, with foundation funding and technical assistance from Johns Hopkins School of Public Health they have built the capacity for interagency collaboration and enacted an ambitious National Tobacco Control Action Plan (Decision No. 1315/QĐ-TTg) for the Implementation of the FCTC. For resource limited health care systems there is an urgent need to demonstrate the cost-effectiveness of interventions to enhance implementation of tobacco use treatment guidelines to support national policies. Therefore, this proposal is timely in that it promises to provide data to support the Action Plan's calls for integrating cessation services into national health and education programs. As stated in their letter of support (see Dr. Phan letter), and in the Ministry of Health's (MOH) 2011 Annual Review, strengthening the national infrastructure to ensure access to evidence-based cessation services is one of the Ministry of Health's (MOH) highest priorities.³⁵ Together, the past 10 years of capacity building and changes in policy have created a strong foundation for the proposed research plan.

The proposed research is significant for its potential to guide large-scale adoption of promising strategies for implementing and disseminating tobacco use treatment guidelines throughout the public health system in Vietnam and will serve as a model for similar action in other South East Asian Countries (SEACs) and the U.S. In September 2011, the UN General Assembly met to address the threat of non-communicable diseases (NCDs) in the developing world which account for about 63% of total deaths world-wide.^{36,37} The meeting highlighted the fact that tobacco use continues to be the leading global cause of preventable deaths related to NCDs. Most of these deaths occur in LMICs, and this disparity is expected to widen further over the next several decades. Of the world's 1.25 billion adult smokers, 10% reside within SEACs. Therefore, it is critical to develop strategies for increasing access to evidence-based tobacco use treatment services that could lead to significant reductions in tobacco related morbidity and mortality. Significance is enhanced by the strong stakeholder commitment and inclusion of a rigorous assessment of the implementation process which will contribute to our understanding of not only what worked but how it worked, thus increasing the generalizability and the potential to inform effective scale-up across the national health system in Vietnam and other SEACs.

C. INNOVATION. This proposal aims to fill gaps in research needed to assess the most effective strategies for implementing tobacco use treatment guidelines in health centers globally and locally. We believe the proposal is innovative in several areas: First, it seeks to shift current approaches to implementing FCTC components by building translation considerations into initial intervention development and study design. We will achieve this goal by building formative and process evaluations into our study design and applying an organizational model for innovation implementation that will provide information needed to facilitate broad dissemination into routine practice.³⁸⁻⁴⁰ Techniques for gathering such data must factor into the conceptualization and evaluation of a study from the start, yet studies rarely do so.⁴¹⁻⁴³ Second, we are aware of only one research project that is assessing the effect of primary care-based cessation interventions in SEACs.⁴⁴ However, that project is focused narrowly on patients with diabetes and relies on stand-alone cessation clinics that are not necessarily a sustainable or generalizable resource. In contrast, and in keeping with the WHO Guidelines for implementing Article 14,¹² this proposal will test a model that leverages existing resources and therefore, if effective, will be positioned for large-scale dissemination. No SEACs have attempted to systematically study strategies for implementing tobacco use treatment guidelines as a routine part of care processes. Third, integration of CHWs into the delivery of health care is a promising model for reducing gaps in preventive services in the U.S. and globally. Yet, we are aware of only one study in the U.S. that tests this model to improve implementation of evidence-based tobacco cessation services, and none in LMICs.^{25,33}

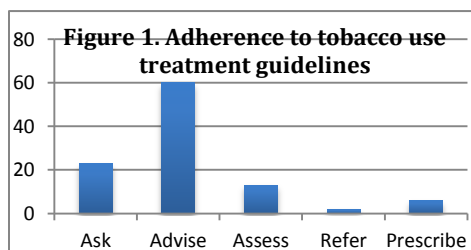
D. APPROACH

D.1. Investigative team and relevant experience. This proposal brings together critical public health stakeholders in Vietnam and a strong multi-disciplinary group of investigators from New York University School of Medicine (NYUSOM) and the Institute of Social Medical Sciences (ISMS), a well-established research institute in Vietnam. The study will be Co-led by Donna Shelley, MD, MPH, NYUSOM (tobacco control and implementation science) and Nam Nguyen, MD, Dr.PH, Director of ISMS (clinical epidemiology, qualitative research, large-scale public health program evaluation in Vietnam). The proposal capitalizes on Drs. Shelley and Nguyen's previous collaboration on a NIH-funded grant (R01CA93788) to test the effectiveness of a multi-component community-based smoking cessation intervention among Chinese immigrants living in the U.S.⁴⁵

Dr. Shelley has extensive experience conducting practice-based research targeted at implementing tobacco use treatment guidelines in a wide range of health care settings including community health centers in the US. (R01CA162035, U01HL105229-01, 1R18HS017167-01, R03HS0160000).^{21,22,45-47} Additionally, over the past nine years Dr. Shelley has been PI of the New York State Department of Health-funded Manhattan Tobacco Cessation Center (<http://pophealth.med.nyu.edu/divisions/mtcp>), which is studying methods for disseminating tobacco use treatment guidelines in primary care settings throughout the State. Dr. Nguyen has considerable experience conducting large-scale quantitative and qualitative research studies in Vietnam (Appendix A for list of funded projects and Resource page for org. chart). As Director at ISMS, he has served as a Principal or Co-Investigator on over 28 research and evaluation studies in Vietnam, employing a broad spectrum of research methodologies and with funding from a wide range of donors such as Abt Associates, USAID/PEPFAR, the Bill and Melinda Gates Foundation, Population Council, PATH, Pact, and World Vision Australia. The current proposal will also profit from Dr. Nguyen's broad network of and collaboration with government officials in Vietnam, District Health leaders, and faculty in partnering academic institutions. The investigative team also includes Dr. VanDevanter (NYU College of Nursing) with expertise in qualitative methods and tobacco control, Dr. Braithwaite, (NYUSOM), with expertise in cost effectiveness analysis, Dr. Islam (NYUSOM, expertise in CHW training and interventions), Dr. Hoang (Co-I Vietnam) an expert in health economics, Dr. Phan a leader in implementing the FCTC in Vietnam (Co-I and Vice Director of the Ministry of Health's Vietnam Committee on Smoking and Health (VINACOSH)), and external scientific advisors Drs. Weiner and Stillman. Dr. Weiner is a leading expert in implementation science and Dr. Stillman has a decade of experience collaborating with Dr. Phan and the Vietnam Ministry of Health to build capacity to implement the full scope of the FCTC.⁴⁸ The feasibility of the research plan is enhanced by the expressed commitment (See letters of Support) of District Health Directors in Vietnam and Scientific and Stakeholder Advisory Committee members dedicated to promoting the treatment of tobacco dependence and disseminating our findings nationally and internationally.

D.2. Preliminary Studies

D2.1.a. Providers and CHWs agree that providing smoking cessation assistance fits well with their roles and responsibilities. Provider survey (Appendix B.1): In November 2012 we conducted in-person surveys of 134 clinicians in 22 community health centers (CHCs) in Dong Anh District of Hanoi to assess attitudes towards tobacco use treatment and the feasibility of the CHW referral model. We adapted a validated tool and pre tested it for relevance and comprehension in one CHC.⁴⁹ A research assistant administered the surveys after obtaining verbal consent, with a 95% response rate. Consistent with national statistics, 80% of the health care providers were female (10% physician, 73% nurse or Physician Assistant). Less than 10% were current smokers and these were all male clinicians. Figure 1. shows that in the past month, only 23% of providers reported screening half or more of their patients for tobacco use, 33% provided advise to smokers, and less than 10% offered assistance (i.e., counseling referral or medication). However, over 90% agreed or strongly agreed that providers can be effective in helping patients stop smoking, but 60% were not aware of the best treatment to help patients stop smoking and only 29% agreed that they had the training needed to help smokers quit. Over 80% agreed or strongly agreed that offering smoking cessation treatment was part of their job and that their supervisor thinks that helping smokers is a priority (Appendix B.2 Survey results) Over 90% agreed or strongly agreed that they would refer patients to a CHW for future counseling and that CHWs could be trained to provide tobacco use treatment. Ninety four percent had not participated in formal training on tobacco use treatment. The most commonly reported barriers to treatment were lack of training (70%), lack of referral resource or additional staff to assist with cessation counseling (69%) and lack of patient interest (80%).



Community health worker focus groups (Appendix B.3 guide): Also in November 2012, we conducted four focus groups with 28 CHWs recruited from the Dong Anh District CHCs to assess attitudes, knowledge and beliefs about tobacco use and their potential role in the proposed referral model. CHWs described tremendous satisfaction with their job. (Appendix B.4 codebook) The position brings prestige and respect from community

members and their colleagues in the CHCs. They are viewed as knowledgeable public health professionals and an important resource for their community as well as for their colleagues in the CHCs. Two key themes, "feasibility" and "support for the concept" delineated participant's endorsement that the CHW referral model fits well with the roles and responsibilities of CHWs who currently work with CHCs as "provider extenders" for many preventive services. Additional themes included "relevant experience" counseling patients on a range of prevention issues including advising smokers to quit. They were confident that they could provide cessation services but viewed a "lack of tobacco-specific knowledge" and a need for additional training as current barriers. *"It is better if CHWs are equipped with knowledge and information so that we will be able to disseminate the right information to the right people."* Another theme was the changing norms, believed to be a result of aggressive counter advertising. However, this was accompanied by frustration that there were no programs to help smokers quit. *"There are warnings on the box, but there has not been any action to help smokers quit."* *"We have not done any workshops regarding to direct propaganda about tobacco cessation to smokers. We have just done some individual counseling to smokers at their houses."* CHWs endorsed the proposed study approach, including the need for individual counseling and home visits. They also agreed that CHWs were the most appropriate health care provider to offer more intensive cessation assistance. *"My colleagues and I feel very happy to do this program. It will help our community."* *"It is more suitable and effective if we rather than people working in other departments give counseling to quit."*

D.2.1.b. From 12/12 through 2/13 we conducted a pilot test of the CHW referral model (ARM 2 of the proposed two-arm study) that demonstrated patient and provider acceptability and the feasibility of this approach. First we adapted and translated a curriculum (Appendix B.5) that is based on the PHS Guideline. We added modules on motivational interviewing, communication skills and roles of the CHW counselor that were adapted from an existing curriculum developed for lay counselors.⁵⁰ We conducted two focus groups (Appendix B.3 guide) with 16 CHWs to evaluate the curriculum. We made changes based on feedback and then conducted a training of all providers (5) and CHWs (6) in one CHC in Dong Anh District, Hanoi. Together with experienced ISMS trainers and Dr. Nguyen, Dr. Shelley conducted a 5 hour training with clinicians and CHWs followed by an additional two-day training with 3 of the 6 CHWs to provide more in-depth training on MI and communication skills, review the counseling manual (Appendix B.6), review the tracking system (Appendix B.7) and to role-play several case scenarios. Using the proposed study protocol for ARM 2, over a one week period, 30 patients were identified as current smokers and 15 agreed to be referred to the CHW for counseling. CHWs were able to contact all smokers who agreed to be referred and enrolled 14 in the counseling protocol. Thirteen of the 14 completed both in person counseling sessions (all home visits, mean 30 min.). At eight weeks post enrollment, 10 patients reported 7 day point prevalence abstinence. Among the remaining four patients, all reported at least one quit attempt in the past 4 weeks. In sum, we demonstrated the feasibility of providers identifying and referring patients for counseling and high rates of participation and retention (93% completing both sessions and 100% completed 8 week in-person surveys). CHWs reported, during post intervention interviews, that patients were enthusiastic about participating and home visits were helpful in also engaging the family in supporting the patient's quit attempt. They recommended lengthening the CHW training to increase skill and confidence in using the manual and adding one more counseling session.

D.2.2. A number of large studies, Dr. Nguyen and ISMS have demonstrated the feasibility of leveraging community health centers in Vietnam to implement and disseminate best practices in preventive services. (Appendix A) For example, since 2009, ISMS has worked on numerous research projects with Alive & Thrive (A&T), an initiative funded by the Bill & Melinda Gates Foundation to improve infant and young child feeding practices in Vietnam. The implementation strategy for A&T is a social franchise model that integrates high-quality nutrition counseling into primary health care.⁵¹ As of 2012, the A&T project has established 780 A&T franchises at CHCs in 15 provinces, covering an estimated 236,000 children. Dr. Nguyen is currently acting as the PI for the A&T process evaluation, which employs mixed methods to evaluate A&T's intervention implementation processes and examine factors shaping the demand and practice of the A&T franchise. ISMS is currently in the field collecting data from health staff, patients, and facilities in 32 CHCs in 4 provinces.

Another example of Dr. Nguyen's relevant previous research is the Primary Health Improvement Initiative-Intervention Phase (PHI-IP) Project. The aim of this project is to improve access to evidence-based reproductive health services. Dr. Nguyen is a Co-PI and is working in collaboration with Population Council Vietnam and Thai Nguyen University of Medicine and Pharmacy. Similar to the proposed study, this project involves a formative assessment of the health care system in Thai Nguyen (one of the proposed study provinces) and includes provider, client, and household surveys to assess practices patterns and health care utilization. As part of this project ISMS has collected data on characteristics of health districts in which we propose to conduct the study. **Table 1.** represents data from the Thai Nguyen assessment, and a recent study ISMS conducted in Hai Ba Trung District, and shows the workforce capacity in the two districts in which we propose to conduct the study.

TABLE 1. Study District characteristics	Population		# Districts	# CHCs	# Health workers	# CHWs
	Male	Female				
Ha Noi (Urban)	3,227,395	3,332,516	29	577	2885	3642
Hai Ba Trung District	185,971	192,028		20	130	156
Thai Nguyen (rural)	568,230	580,870	9	180	980	1136
Pho Yen District	72,868	73,034		18	96	334

Relevance: These are just two examples of ISMS's capacity to conduct large-scale, rigorous research related to the proposed study aims. We will leverage networks and resources developed through these previous projects.

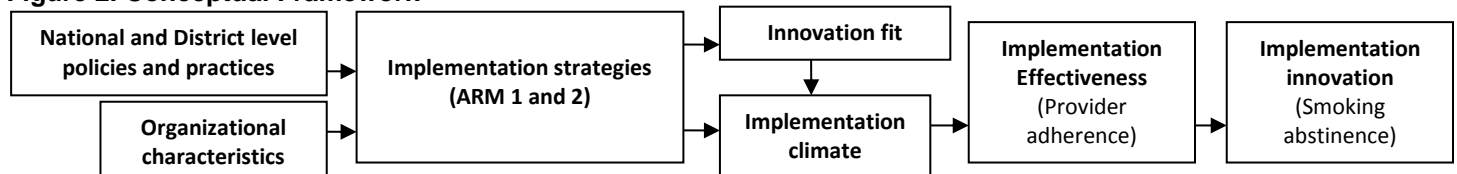
D.3. Research Plan

D.3.1. Overview. We propose to conduct a formative evaluation (**AIM 1**) to assess the contextual factors of the intervention settings (district level policies and organizational level characteristics) that may influence tobacco use treatment in CHCs and to inform additional modifications to the proposed implementation strategies. We will then conduct a two-arm randomized control trial (**AIM 2**) to compare the effectiveness and cost effectiveness of two multi component implementation strategies: ARM 1- technical assistance, training and a clinical reminder (TTC) vs. ARM 2- TTC plus a community health worker (CHW) referral system. (Figure 3) The primary outcome is improvement in provider adherence to tobacco use treatment guidelines (defined here as implementation effectiveness) which has been found through extensive meta-analysis to be an essential determinant of patient cessation outcomes.⁸ The secondary outcome is six-month biochemically verified smoking abstinence rates. Finally, guided by Weiner's organizational model of innovation implementation, we will explore external (e.g., national and district level policy) and organizational factors that may influence the relationship between the implementation strategies and implementation effectiveness (**AIM 3**).^{38,39,52-56}

D.3.2. Conceptual framework. (Figure 2) Our proposed study draws on an organizational model of innovation implementation that Weiner et al. (Consultant) has tested and refined in prior work, including a current R01 study (5R01CA124402-05).^{38,39,53} Briefly, the model posits that the primary and secondary outcomes of **implementation and innovation effectiveness** are a function of the **implementation strategies** (i.e., training, technical assistance, chart reminder and CHW referral) which are employed to support guideline adherence. The model further posits that these implementation strategies enhance implementation effectiveness *through* changes they produce in the **implementation climate** and the extent to which providers perceive that delivering guideline-concordant tobacco use treatment **fits their values and local task requirements** (e.g., clinic workflow and workload).

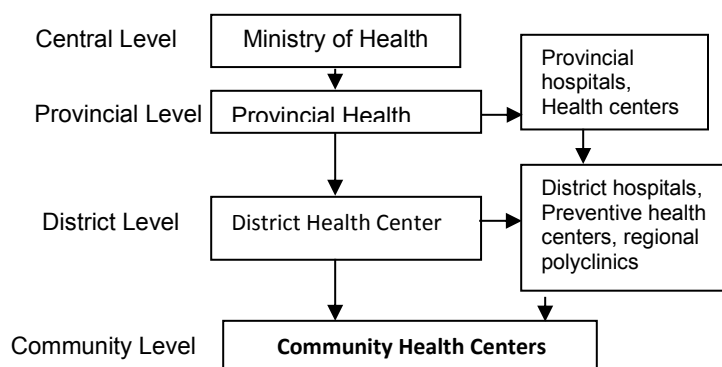
Implementation climate is further defined as the extent to which providers perceive that guideline adherence is a *priority* (i.e., it is expected) and is *supported* (i.e., providers have the means and opportunity to adhere to guidelines). ARM 1 (TTC) is expected to promote a positive implementation climate by enhancing providers' perception that tobacco use treatment is a *priority* and by providing the *means* (i.e. new knowledge through training) for adhering to guideline recommended care. We hypothesize that the addition of a CHW referral system (ARM 2) will result in provider adherence levels that are superior to ARM 1 through additional changes in perceived *means, opportunity and enhanced task fit* (i.e. referral system offers providers' an opportunity to delegate counseling and follow-up). We will augment the proposed model by placing it within an ecological framework which acknowledges that in addition to organizational level factors, the potential for large scale implementation and dissemination of evidence-based practices will be influenced by proximal factors including external policies and regulations within the larger health care system in Vietnam.^{52,54}

Figure 2. Conceptual Framework



D.3.3. Study Setting: Vietnam health care system. The Vietnamese health care system is hierarchically organized into four administrative levels: central, province, district and community (**Figure 3 and Appendix C**). At the central level is the Ministry of Health (MOH), the main national authority in the health sector which formulates and implements national health policies and programs. The provincial-level health system consists of Provincial Health Departments and Preventive Health Centers, which are administered by the Provincial People's Committee in each province. Each province has at least one general hospital. At the district level, the District People's Committee administers district health centers and district-level hospitals. Within districts the **community health centers (study sites for this proposal)** serve as the primary access point for public health and preventive care services in Vietnam, each providing services for an average of 5000-7000 people in their surrounding community.

Figure 3. Vietnam Health



CHCs are charged with implementing 10 national health programs, treatment of common diseases, provision of health counseling and education, referral services, pre- and post-natal care, family planning, and food hygiene and safety. Each CHC is staffed by 5-6 clinicians, including one physician and three to five other health professionals (physicians, nurses). In addition, each CHC is supported by a network of 8-10 community health workers (CHWs) who primarily conduct outreach work in the villages or wards within a CHC. There are more than 100,000 CHWs active in preventive medicine at the community level. CHWs have five main

responsibilities: 1) delivering health information; 2) delivering counseling on disease prevention; 3) promoting maternal and child health and family planning; 4) providing first aid care and basic treatment for common diseases; and 5) implementing national health programs at the village level. CHWs are under the direct management and direction of the CHCs and coordinate with community and social organizations in the village. In terms of access to care, patients receive free care at CHCs if it relates to the 10 national health prevention priorities. In addition, the Health Care Fund for the Poor directly pays services at CHCs for eligible recipients (i.e., poor, children under 6 years of age, students, elderly, and socially protected groups including ethnic minorities). As of 2010, the Vietnam subsidizes 50% of the insurance premium for near-poor families. In 2010, the proportion of people covered by health insurance was 60%, 42.7% of which was health insurance for the poor.⁵³ CHC's focus on preventive care, their role as the first access point for the health care system and the availability of services at no cost to a large majority of the population makes them the ideal setting for implementing tobacco use treatment guidelines. Notably, the MOH's 2011 Annual Health Review included information on several international projects in Vietnam aimed at creating "care pathways" to improve implementation of treatment guidelines into routine practice and emphasized the need to strengthen capacity to implement best practices in district and community-level health care settings.³⁵

D.3.4. AIM 1 To conduct a formative evaluation.

D.3.4.a. Study Design. The formative evaluation has three components: 1) Key informant interviews with leaders in the public health sector responsible for developing and implementing policy in Vietnam to assess contextual factors (e.g. district level policies) that may influence implementation and dissemination; 2) Focus groups with current smokers to inform adaptations to the current training curriculum and counseling manual; and 3) baseline study site assessments to assess organizational readiness to change and current policies and practices to inform necessary adaptations to the proposed system changes. Working with Dr. Nguyen and colleagues we will develop semi-structured interview and focus group guides and adapt survey tools guided by the conceptual model described above as well as a robust literature on factors that influence implementation and dissemination.⁵⁰⁻⁵²

D.3.4.b. Data collection. 1) Key informant interviews. We will conduct key informant interviews with at least one senior level staff person from the following stakeholder groups: a) MOH central level agencies involved in tobacco control such as VINACOSH, and the Ministries of Education and Training and Science and Technology; b) Executive Directors of the Vietnam Medical Association and the Vietnam Public Health Association; c) WHO Vietnam; d) at the provincial level, a representative from the Department of Health and Preventive Medicine Center; and e) four district health directors in the two target provinces (HaNoi and Thai Nguyen) for a total of about 16 interviews. We will use a semi-structured interview guide organized by constructs found to influence implementation and dissemination outcomes.⁵²⁻⁵⁶ These include external factors (tobacco control policies, national priorities for resource allocation and relative priority of tobacco control, relative priority of smoking cessation) perceived barriers to implementing guideline recommended cessation services, perceived commitment of leadership in and outside the MOH, perceived challenges to maintaining and disseminating changes in service delivery at the local and province level. Recruitment for key informant interviews: Using a purposive sampling approach, Dr. Phan (Co-I, and Vice Director of VINACOSH) and ISMS will leverage their contacts to assist in recruiting stakeholders for the key informant interviews through email invitations to participate. Research staff will then follow-up by telephone to enroll stakeholders in the study. Dr. Nguyen and Dr. Pham will conduct these interviews.

2) Focus groups: An experienced facilitator from ISMS will conduct six focus groups (3 in each study district) with current smokers (6-8 participants, 4 male and 2 female groups). The focus groups will assess

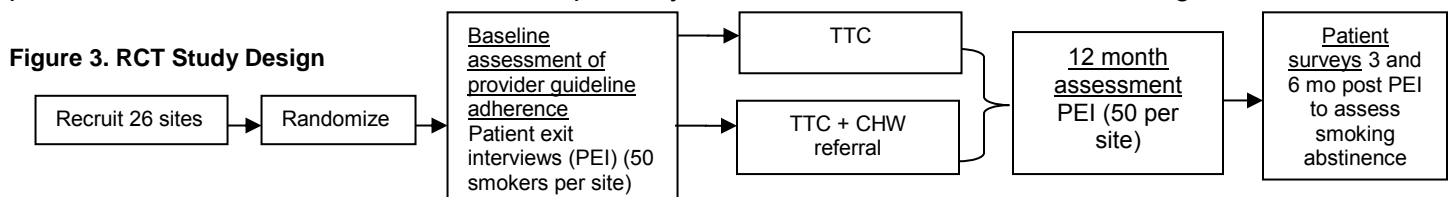
expectations about health benefits of quitting, past cessation history, including availability, affordability and use of cessation medications, knowledge of cessation resources, and attitudes towards the proposed intervention. There is a relatively large database on the knowledge and attitudes about tobacco use among smokers in Vietnam.¹ Therefore, the groups will focus more on access to treatment, attitudes towards pharmacotherapy and treatment preferences. Inclusion/exclusion criteria include: current smoker (smoked in past 7 days), patient of a CHC in one of the two study districts, and age 18 and over. Recruitment for focus groups: We will use the same method as we used to recruit patients to the pilot study. Patients will be screened for current tobacco use in the CHCs, asked to participate if they meet eligibility criteria and given a date and time for the meeting. We will obtain consent at the time of the focus group.

3) Baseline study site assessments: In all enrolled study sites we will conduct the following: **a)** an assessment of baseline organizational characteristics. This includes data on setting-level variables shown to influence the implementation of practice guidelines including number of FTE staff, clinic volume, policies and systems.^{54,55} We will use a practice environment checklist to inventory current policies, workflow, systems (e.g. chart systems) and staff roles and responsibilities in general, and specifically related to tobacco use treatment. **b)** Semi-structured interviews (Appendix D.1) with clinical and administrative key informants (clinical director, 2 CHWs and 3 providers per site) to supplement the checklist data and to elaborate on potential barriers and facilitators for tobacco use treatment. **c)** A provider and CHW survey (Appendix C.1) (tested in the pilot research and based on a survey from the WHO that was validated in Vietnamese).^{49,57} Surveys will assess baseline knowledge, attitudes and current practice patterns related to tobacco use treatment to inform additional modifications in training materials. **d)** Organizational readiness to change: provider surveys will include the Change Process Capability Questionnaire (CPCQ) (Appendix D.2), a validated tool that is applicable to primary care practice.⁵⁸ *Site recruitment procedures are described in Section D.3.5.b.* (see Table 2 for measures and data collection)

D.3.4.c. Data analysis. Qualitative data obtained from the audio recordings of the semi-structured interviews and focus groups will be transcribed verbatim in Vietnamese by ISMS and then translated. The analysis will be led by experienced qualitative researchers (VanDevanter and Nguyen). Dr. Nguyen's fluency in English and Vietnamese will address concerns about ensuring "conceptual equivalence."^{59,60} To facilitate data analysis data will be entered into NVivo qualitative software. Data coding will begin with the reading of the transcripts by Drs. Nguyen and VanDevanter to identify preliminary codes. Data analysis will consist of a three-level coding process: open coding to identify relevant patterns in the interviews, followed by focused coding to identify clustered concepts and to organize ideas, and finally identification of major themes.⁶¹⁻⁶³ A coding manual will be developed and finalized by Drs. Nguyen and VanDevanter in an iterative process. All transcripts will then be independently coded by Dr VanDevanter and another member of the research team to establish inter-rater reliability. Quantitative data will be summarized using means, medians and other quantiles, standard deviations, interquartile range, minimum and maximum, as well as graphically (e.g., boxplots).

D.3.5. AIM 2: To compare the effectiveness and cost effectiveness of two implementation strategies to increase adherence to tobacco use treatment guidelines, and AIM 3: To explore organizational factors hypothesized to influence the relationship between the implementation strategies and implementation effectiveness. We will combine these Aims for the remainder of the Approach section because of overlaps in design and data collection.

D.3.5.a. Study design. We will conduct a two arm, randomized trial comparing: ARM 1) technical assistance, training, and clinical reminder system (TTC), and ARM 2) TTC+ referral to a CHW for additional counseling and follow-up. We will conduct a baseline assessment of provider adherence to tobacco use treatment by collecting patient exit interviews (PEIs) (i.e., surveys conducted immediately after the patient visit) from 50 patients per site who meet eligibility criteria as current smokers. We will then implement the components of ARM 1 and 2. At 12 months post implementation we will conduct PEIs with another 50 smokers per site. These patients will be asked to consent to follow-up surveys at 3 and 6 months to assess smoking abstinence.



D.3.5.b. Study site eligibility and recruitment: We have chosen two provinces to represent both an urban and rural setting. Based on Dr. Nguyen's recent assessment; Thai Nguyen has 9 districts with 180 CHCs and Hanoi (urban) has 29 districts with 577 CHCs. We have preliminarily selected one district from each province for inclusion in the study. The district we have selected in Hanoi is representative of those CHCs located in the

central part of the city and the district in Thai Nguyen is representative of the rural CHCs in that province. Site criteria include having at least one physician, ≥ 4 allied health care professional staff, ≥ 5 CHWs and a patient population of at least 4000. Using methods for site recruitment used by ISMS, the Director of the District Health Centers will introduce our study to all CHCs that fit these criteria through a letter of introduction and follow-up telephone or in person contacts. Among those expressing interest, we will randomly select 26 CHCs (13 rural and 13 urban). Sites will be randomly assigned in a 1:1 ratio to the intervention conditions within urban and rural strata. We will recruit sites in 3 successive waves (see timeline in budget justification).

D.3.5.c. Intervention conditions

ARM 1: Technical assistance, staff training, and clinical reminder system (TTC)

Technical assistance (TA): Prior to beginning the intervention, the research team will meet with the providers and site project leader (“champion”) at each CHC to review participation requirements and discuss project logistics. We will train two program coordinators as “outreach specialists (Specialists)”. They will undergo a 4 day training adapted from ISMS curriculum used for similar projects and curriculum guidelines for practice facilitation.⁶³ The training will focus on quality improvement methods, system tools for tobacco use treatment, evidence-based guidelines and group facilitation and communication. Each Specialist will be responsible for a maximum of 6 clinics at any given time during the grant period. Dr. Pham (MD, Project Manager) and Dr. Nguyen will meet weekly with Specialists to provide supervision and to review weekly activity reports. Guided by protocols used in our own work and in the literature, we will provide technical assistance to all study sites.^{17,32,65-67} Specialists will make monthly sites visits months 1-2 and then at 3 and 6 months to meet with the site leaders. The purpose of outreach visits will include observations of clinic operations, additional staff training and as needed, problem identification and brainstorming, and provision of materials and resources. Specialist will also pay attention to how the addition of tobacco use screening and treatment guidelines impacts other care processes and prevention priorities. They will be provided with a checklist to standardize the visit activity.

Staff training (Appendix B.5): All clinical and support staff will attend a one day training in the use of the 5As and the intervention protocol, including how to make a referral to the CHW. The training is based on the PHS Guideline *Treating Tobacco use and Dependence*. Trainings will be conducted by Dr. Shelley and Dr. Nguyen. Consistent with well-established treatment fidelity recommendations we will standardize provider training and evaluate the adequacy of training by measuring provider skill acquisition post-training through the observation of role play of hypothetical case vignettes.⁶⁸ We will also conduct pre and post surveys to assess changes in knowledge and to assess satisfaction with the training. ISMS staff and Dr. Nguyen have translated the training materials from English to Vietnamese and sections have been modified based on the pilot research described above. The training program will be made available online to address potential staff turnover and increase potential for dissemination.

Clinical reminder system: The chart system is designed to remind the intake clinician to assess smoking status, assess readiness and to offer each smoker brief cessation advice. To enhance uptake and sustainability, the chart prompt (Appendix E) will be integrated into the existing chart system. We will also develop and adapt additional office tools which will include language concordant materials that will reinforce training and technical assistance (i.e., a pocket card with scripts and patient self help material) (Appendix E).

ARM 2: TTC+ referral to CHW

Referral to CHW. The baseline site assessments will inform the final design of a seamless system for providers to make referrals to the CHWs. However, based on our pilot research we propose to create a referral form that is similar the one we have tested in the U.S. (Appendix E).^{21,22} For smokers who are interested in quitting and agree to be referred for counseling, the form will be completed by the CHC staff. CHWs will then pick up the forms at their regular weekly meetings at the CHCs. Smokers will be contacted within five days of their visit to schedule the first of three counseling sessions (Appendix B.6 Counseling Manual). These sessions will last approximately 30 minutes and will be conducted either in person or by phone. The first session will be conducted within one week of the patient visit to the CHC (planning session) and the second and third sessions at 2 (within 2 days of quit date) and 4 weeks post clinic visit. The counseling schedule is based on the PHS Guideline, our pilot data, and evidence that early more intensive contact around the quit date is associated with improved cessation rates.^{69,70} Counseling will focus on motivational barriers for treatment readiness and offer stage-based cessation advice. Motivational interviewing (MI) techniques have been found to be effective in increasing abstinence and quitting attempts.⁷¹ There is also evidence that lay health workers can be trained to offer effective MI.⁵⁰ Four CHWs from each intervention clinic will be invited to participate in a four-day training that will build on the provider training to include a theory-based interactive approach to ensure proficiency in motivational techniques. The MI module was adapted from an existing curriculum and pretested

in two focus groups with CHWs.⁵⁰ Standardized training, setting performance criteria and conducting booster sessions will help ensure intervention fidelity. In addition, each CHW will have a field manual which will have all of the information necessary for completion of the intervention components as well as a checklist to complete for each patient interaction (Appendix B.7). CHWs will receive ongoing supervision by means of bimonthly meetings with trained ISMS staff and will attend a booster training session two weeks after the intervention begins to minimize drift in counseling skills. The follow-up meetings will be problem-based and focused on discussion of challenges in the field. CHWs will provide feedback on their interaction with the patient to the referring provider. This “consultation” form will be placed in the patient’s chart to provide a record of the contact. Typically we audiotape counseling sessions to assess fidelity. However, in this setting we will adapt an approach used by Dr. Nguyen in previous research. At the start of each week, CHWs will provide a schedule of home visits to the RA. The RA will observe a random selection of the counseling sessions and document delivery of essential components of the CHW protocol.

D.3.5.d. Data collection and measures for AIM 2 and 3. Our assessment plan is intended to compare the effectiveness and cost-effectiveness of two strategies for implementation of the tobacco use treatment guidelines (AIM 2) and to examine, theory-driven mechanisms hypothesized to explain the effectiveness of the two strategies (AIM 3) in public health clinics in Vietnam. Mixed methods (i.e., interview and survey) data will be collected from providers and CHWs. For clarity, our assessment plan is organized according to following domains: Primary Outcomes, Secondary Outcomes, Cost Measures, Baseline Organizational Characteristics, Implementation Fidelity and Implementation Climate. **(Table 2)**

D.3.5.e. Outcome evaluation (AIM 2)

Primary outcome: Adherence to tobacco use treatment guidelines (Implementation Effectiveness): To assess the primary outcome of provider adherence to tobacco treatment guidelines, we will conduct patient exit interviews (PEI) (surveys conducted immediately after the patient visit) with 50 smokers pre and 50 post-implementation at each site (1300 in each study period). We will pilot test and adapt a validated tool for measuring the primary outcome.⁷² (Appendix F.1) Studies conducted in the U.S. demonstrate that patient questionnaires conducted at the point of service are considered to be the optimal non observational method for measuring provider delivery of tobacco use treatment outpatient treatment.⁷³⁻⁷⁵ The PEI, completed immediately after the visit, assesses the full spectrum of PHS guideline recommended care (i.e., 5As). It has well-established validity as evidenced by strong correlation with more costly audiotaped assessment of physician-patient interactions ($r=.67$, $p<.001$).⁷² Prior to, and approximately 12 months following each site’s enrollment, consecutive patients will be screened in the waiting area prior to seeing their clinician, to determine smoking status and to obtain consent for the exit interview. The PEI will also assess readiness to quit⁷⁶ and patient demographics. Patient eligibility includes: 1) age 18 or over; 2) at the CHC for a routine patient visit; and 2) active smokers (current smoking within the past 7 days). Based on data from the district health centers and our pilot research the study sites have about 50 adult patient visits/day, 35% of which are males and about 46% of men are current smokers (~8 eligible patients/day). We estimate that 40% will be willing to participate (3/d) and thus expect to be able to enroll the number needed (50/site) within the projected timeline (4-6 wks/site).

Secondary outcome: Using accepted standards for measuring cessation outcomes,⁷⁷ all patients who complete a PEI in the post intervention period will be followed prospectively to assess 3 and 6 month 7-day point prevalence abstinence, defined as any smoking (even a puff) in the past 7 days. Surveys will be conducted in person and smoking abstinence will be validated using carbon monoxide (CO) monitoring with abstinence defined as a $CO<10ppm$.⁷⁷

Measures for CEA: *Cost measures* include implementation costs (CHW, system changes), patient time costs and medical costs including model-estimated impacts on downstream costs attributable to tobacco-related illness (e.g. myocardial infarction). Health care and staff salary cost estimates will be derived from Vietnamese health ministry officials (letter Phan). Implementation costs will include health professional time requirements (including training of clinicians and CHWs), major constituents of the CHW intervention (e.g., time, travel, durable equipment) and patient and provider materials. Incremental patient costs will be assessed by surveying additional patient time required by the CHW, as well as any indirect costs that are required (e.g. elder or child care). We will develop templates to capture data prospectively and to improve accuracy of the cost assessment.⁷⁸ *Effectiveness inputs* for the simulation will arise from Aim 2 and will include 6 month smoking abstinence and changes in health-related quality of life as measured by the EQ-5D which has been translated into Vietnamese.⁷⁹ We will explore variable assumptions regarding the persistence of abstinence (e.g. relapse) in sensitivity analyses. Estimates regarding baseline disease incidence of chronic lung disease, lung cancer, and myocardial infarction, as well as lifetables describing all-causes mortality stratified by sex will be based on Vietnamese data. Our costing methodology will be particularly robust because we will utilize our survey of baseline organizational characteristics (see AIM 1) and interviews to assess current practice patterns

specifically related to tobacco use treatment; and our fidelity measures (see below) will provide data on all implementation activities.

Baseline organizational characteristics: See AIM 1 formative assessment and Table 2.

Implementation fidelity. We will use several approaches to evaluate the extent to which each component of the implementation strategies was delivered as intended.^{43,80}

Technical assistance, training and office systems: Outreach specialists will use checklists and logs to document the number, frequency and duration of outreach contacts and contact purpose. RAs will conduct site visits at 2, 6 and 12 months to document (using a checklist) that the reminder and referral systems and other system tools were put into place. We will record the percentage of staff who attend the trainings, as well as any changes in staffing, and we will conduct brief pre and post training assessments.

Referral system: Using the patient exit interviews (PEI), we will measure the percentage of eligible patients who received a referral to the CHW (patients ready to quit and agreed to referral which is assessed in the PEI). We will also track the number of completed referral forms. We will measure the percentage of patients referred who were reached by the CHW and the number of contacts CHWs made with each patient contacted using CHW logs.

Implementation Climate and Innovation Fit. (AIM 3) We have adapted a survey tool developed by Weiner to measure these constructs.³⁹ (Appendix F.3) Implementation climate is assessed with 13 questions that assess providers' perceptions about the extent to which use of the innovation (in this case implementing tobacco use treatment guidelines) is expected, supported and recognized (e.g. "I get the support that I need to treat patients who smoke.") Values fit and task fit are each measured with three questions. We will administer the survey pre and post implementation (12 months). Implementation climate is an organization-level construct, therefore, we will test whether sufficient within-group agreement exists to aggregate individual responses to the clinic level.^{81,82} If tests do not justify aggregation, we will examine intra-clinic variability in climate perceptions.⁸¹

We will also conduct semi structured interviews post implementation with a sample of study participants in each site (2 CHWs, 3 providers and 1 site leader). These data will supplement the quantitative data collected in the provider survey by allowing us to explore, in more detail, the patterns we observe from the quantitative survey, thus providing a synergistic understanding of factors that influence the study outcomes.⁸³ We will use the qualitative guides that were used in the baseline site assessments but they will be adapted to obtain more detailed data about the process of integrating the implementation strategy into the workflow and customizing it to the study settings, site-specific barriers and facilitators of strategy implementation and information about the implementation strategies themselves, including satisfaction with the amount and quality of training and technical assistance provided and with the office system enhancements. The survey and interviews will be administered by the RA using a paper survey tool and semi-structured interview guide.

TABLE 2. Measures, data sources and data collection

CONSTRUCTS	MEASURES	DATA SOURCES	TIMING	AIM
PRIMARY OUTCOME: Implementation Effectiveness	Provider adherence to treatment guidelines	Patient exit interviews ⁵⁹ (Appendix F)	Baseline and 12 months following implementation	2
SECONDARY OUTCOME: Innovation Effectiveness	Smoking abstinence	Patient surveys (Appendix F)	3 and 6 months post PEI in the post implementation period	2
COSTS	Resources associated with tobacco use treatment implementation (staff, health care and patient costs)	Cost collection template Ministry of Health	Ongoing	2
ORGANIZATIONAL CHARACTERISTICS	Organizational change capacity ⁵⁸	Provider survey (Appendix D)	Baseline	2 & 3
	Organizational structure (e.g. FTE, patient demographics) and function (i.e. workflow)	Practice environment checklist and semi structured interviews	Baseline	2
IMPLEMENTATION FIDELITY				2
Technical assistance	<ul style="list-style-type: none"> Number, frequency, and duration of outreach contacts, contact purpose % of staff attending trainings at each site, quality of training, and knowledge acquisition Evidence chart system and materials are in use and onsite % eligible patients referred, # patient contacted and sessions completed 	<ul style="list-style-type: none"> Outreach logs and Provider interviews Training log, trainee evaluations Site observations PEIs, CHW checklist, referral forms 	Implementation period and Post implementation	
Trainings				
System change				
CHW referrals				
IMPLEMENTATION CLIMATE	Climate and fit instrument ³⁹ (Appendix F)	Provider and CHW surveys and semi-structured interviews	Baseline and 12 months Post implementation	3

D.3.6. Analysis plan

AIM 2. Compare the effectiveness of: 1) Technical assistance, training and clinical reminder system (TTC) vs. 2) TTC + referral to community health worker (CHW). Primary outcome: Data from primary outcome measure will be evaluated using mixed-effects regression analysis to estimate the difference between treatment conditions adjusting for the clustering effects across multiple levels (patients, providers, clinics) of the hierarchical data structure.⁸⁴ Treatment condition differences after the intervention period will be examined by creating a dummy variable for study arm with the TTC condition as reference category. The fixed-effect coefficient for treatment condition will contrast TCC+CHW and TTC alone conditions after the intervention period. Covariates such as baseline organizational factors (guideline adherence, FTEs) and urban vs. rural site, will be considered for inclusion in the mixed-effects model to reduce the within-group variance, if they are predictive of the primary outcome. A complex error term will be specified with intercepts randomly varying across sites and providers within sites. The secondary outcome is smoking cessation, a binary variable (scored 1 = Yes, 0 = No). We will conduct an intent-to-treat analysis (i.e., those lost to follow up considered smokers). The basic model again involves a comparison of the two implementation strategies (CHW+TTC vs. TTC). The binary outcome will be modeled by a generalized linear mixed-effects model⁸⁴ similar to what was described above for the primary outcome. A binomial family distribution and logit link will be used. Exponentiating the fixed-effects coefficient for treatment condition will generate an estimate of the odds ratio (i.e., the effect of treatment condition on the odds of patient smoking cessation).

Power: For the primary outcome, Optimal Design⁸⁵ was used to estimate power to detect an effect size of one standard deviation.⁷² We assume 10 patients per clinician, 5 clinicians per site, and, conservatively, 33% variance (i.e., the intra class correlation or ICC) at each level (site, clinician, patient). With 26 sites, and assuming a two sided type-1 error of 0.05, power is approximately 0.95 to detect this effect size. Optimal Design was also used to estimate power for the secondary outcome, where an odds ratio of 2.3 is expected (13% vs. 26% abstinence for TTC and TTC+CHW conditions, respectively).⁸ We assume a plausible interval for the smoking cessation rate among patients in the TTC alone condition ranging from .01 to .25, and we assume conservatively that 50% of the variability in cessation rates is between clinicians. With 26 sites, we have 80% power to detect the estimated effect size.⁸

Implementation fidelity evaluation. Using the indicators described Table 2, we will summarize relevant data describing the observed implementation of the intervention strategies so as to support reporting of trial outcomes data consistent with CONSORT guidelines modified for pragmatic practice-based trials.⁸⁶ We will use descriptive statistics to assess all fidelity measures including how much and what type of support they received and the reach of the CHW referral program.

Cost effectiveness analysis (CEA): To increase policy impact, Dr. Braithwaite (Co-I and international expert on CEA) will collaborate with Dr. Hoang (health economist Hanoi Medical University and Co-I) to develop a predictive economic model of expected health and cost outcomes associated with smoking cessation among Vietnamese smokers.^{87,88} These data will provide benchmarks for health policy decision-making on allocation of resources for treatment of tobacco dependence in CHCs in Vietnam.

Our approach to assess the value of the addition of a CHW referral system in ARM 2 (TTC+CHW) compared to system changes, technical assistance and training alone (TTC) (ARM1) involves estimating the incremental cost-effectiveness of ARM 2 compared to ARM 1 (i.e., the ratio of its incremental costs to incremental benefits). The incremental cost-effectiveness ratio (ICER) is defined as the incremental change in costs divided by the incremental change in effectiveness (e.g., QALYs with TTC+CHW minus QALYs with TTC alone). "QALY" refers to quality-adjusted life expectancy, and is a quantitative measure that simultaneously takes into account both quality and quantity of life. We will use primary data collection and measures of effect based on analyses from this study combined with mathematical modeling to inform the derivation of the cost and QALY estimates over longer time horizons than those over which data will be collected (5-year, 10-year, 20-year, and lifetime horizons). Downstream impact of TTC+CHW on future costs and benefits (e.g., the downstream health impact of averting chronic lung disease, as well as the downstream costs averted by preventing those diseases) will be assessed via mathematical modeling using a Markov ("state-transition") computer simulation that will enable attribution of the health benefit that would be caused by specified reductions in smoking. This model will be constructed in accord with the methods used by Dr. Braithwaite's modeling team in constructing published policy models for other diseases, including HIV, hip fracture, etc.⁸⁷⁻⁹⁰

We will perform the analysis from both a societal perspective and from a payer perspective, to provide results relevant to the health care system.⁹¹ We include a standard discount rate of 3% for costs and benefits.⁹¹

Sensitivity analyses and uncertainty. In addition to varying each input across its plausible range to assess whether the cost-effectiveness of CHW is sensitive to particular assumptions regarding its value, we will estimate 95% confidence intervals around point estimates of incremental cost-effectiveness using probabilistic

sensitivity analyses in which vectors on the cost-effectiveness plane are identified corresponding to the 2.5th and 97.5th percentiles of incremental cost-effectiveness. We will also create corresponding acceptability curves, which denote the probability that a particular program or programmatic decision is favorable given a particular willingness to pay for health benefits.

AIM 3. Explore theory-driven constructs that may influence the relationship between implementation strategies and implementation effectiveness. For quantitative analysis, mixed-effects models for Aim 2 will be expanded to include additional main and interaction effects. A mixed-effects model also will be estimated for implementation climate and fit with providers' values and tasks, to determine whether treatment conditions were different on the hypothesized mediators. These hypothesized mediators also will be added to the models for Aim 2, to determine whether climate and fit with providers' values and tasks have unique effects on outcomes, after controlling for treatment condition and covariates. Baron and Kenny's⁹² causal-steps test can be applied to explore if the impact of implementation strategies on guideline adherence operates through implementation climate and/or innovation fit. Multilevel structural equation modeling also will be employed to estimate indirect effects of treatment condition on guideline adherence.⁹³⁻⁹⁶ Effect modification by baseline site (i.e. organizational readiness) characteristics will be explored by adding interaction effects between potential modifiers and treatment condition. When any interaction effects are significant, simple main effects of treatment condition, at different values of the modifier, will be examined to determine the nature of effect modification. Qualitative data will be analyzed as described in **D.3.4.c**.

D.4. DISSEMINATION. We propose five main strategies for implementation and dissemination: **1)** After study completion, we will meet again with key informants interviewed as part of the formative evaluation to share findings and explore concrete actions needed for dissemination. **2)** Publications and presentations at national and international conferences including the annual Society for Research on Nicotine and Tobacco conference, regional meetings, and the World Conference on Tobacco and Health. **3)** Local and regional workshops with District Health Directors and relevant local public health professionals to disseminate findings and in Year 5, we will co-sponsor a regional conference with the South East Asian Tobacco Alliance and other stakeholders (e.g. WHO Vietnam) to provide a platform for presenting research from across the region, discussing progress in this region toward reaching the FCTC goals and planning for future collaborations. **4)** Develop an implementation manual (i.e. how-to manual) and dissemination plan.⁹⁷ This document will provide CHCs with step-by-step guidance to help them implement tobacco use treatment guidelines as a routine part of primary care practice. **5)** Develop a Train-the-Trainer Model (TTT) to ensure dissemination of the intervention. Building on Dr. Nguyen's extensive experience creating and implementing TTT models for health care professionals throughout Vietnam (Appendix A) and Dr. Shelley's 10 year training experience associated with her state funded Cessation Center, we will develop a Tobacco use Treatment TTT model that will create a cadre of health care professionals with expertise in population and individual approaches to smoking cessation. Of note, we have chosen to evaluate implementation strategies that are likely to be replicable and sustainable. The system changes (e.g. reminders, referral pathways), tailored to the context of each site, will ensure that tobacco use screening and treatment are integrated into routine care. We will create a tracking system to track outcomes for all dissemination activities (e.g. number of trainings and workshops, number and characteristics of attendees, evaluations of the trainings, etc).

D.5. POTENTIAL LIMITATIONS. First, in order to assure adequate power for achieving the primary and secondary outcomes, we will need to recruit 26 CHCs. We have obtained letters of support from the District Health Center Directors. In addition, Dr. Nguyen has extensive experience conducting research in these CHCs throughout Vietnam. As per Dr. Nguyen's past experience, it is the support of the District Health Center Directors that is critically important for site recruitment, therefore we have not obtained letters from individual sites. Second, we have defined the core elements of the implementation strategies; however, we acknowledge that adaptations to the unique practice context will be necessary. We will use fidelity checks to ensure that the core elements are implemented and will document adaptations to enhance external validity. Third, differences between high income and low-income health care systems, including the high smoking rates among male physicians and lack of cessation medications may pose challenges for implementation. Our pilot research was consistent with national surveys that found that smoking rates among women (nurses and doctors) is less than 5%.¹ Moreover, as our survey demonstrate, over 70% of providers working in CHCs and 90% of CHWs are female. Moreover, there is good evidence that brief counseling alone from a physician or other health care professional, can increase abstinence rates by 30% and more intensive counseling, even without medication, can result in quit rates of >20% at 6 months compared to less than 5% without treatment.⁸ With the increasing burden of tobacco-related chronic disease in LMIC countries, beginning to address this issue through institutionalizing best practices in tobacco use screening and treatment is imperative.

TIMELINE. See budget justification for detailed timeline.