

APPROVAL

July 18, 2024

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Dear Dr. Wang:

The IRB reviewed the following submission:

Type of Submission:	Modification and Continuing Review
Review Type:	Expedited
Study Title:	Adapting effective mHealth interventions to improve uptake and adherence of the HIV pre-exposure prophylaxis (PrEP) in Thai young MSM
Submission Short Title/Nickname:	Thai MSM PrEP Use Project
Principal Investigator:	Bo Wang, PhD
IRB ID:	MODCR00000926
Related Study ID:	H00023523
Funding:	NIH-NATIONAL INSTITUTES OF HEALTH, Grant Office ID: 1R34 MH124081-01A1
IND, IDE, or HDE:	None
IRB Review Date:	7/18/2024
Documents Reviewed:	• Adervse Event log 060821.docx • clinician interview guide 071421.docx • Data Safety Monitoring Plan 051621.docx • Interview Guide_Thai R34 060921.docx • Protection of Human Subjects 09 02 20.pdf • R34 acceptability scales 050624.docx • R34 aim 1 consent form 7.22.21.pdf • R34 aim 2 consent form 7.27.21.pdf • R34 and R21_R33 Thai Translator statement..pdf • R34 exit interview 050624.docx • Revised ISP 5.6.24.docx • Thai R34 Aim 2 questionnaire 050924.docx • Thai R34 proposal 090820 (IRB052021).pdf

	• Thailand_R34 IRB amendment.pdf • Thailand_R34 IRB approval.pdf • Thai-translated_R34 acceptability scales 050624.docx • Thai-translated_R34 acceptability scales 050624.docx • Thai-translated_R34 exit interview 050624.docx • R34 3rd DSMB Letter_Nov2023.pdf • R34 2023 Progress Report.pdf
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This research is reviewed under the 2018 regulations. The study has been given a three-year approval period. Please be aware of the expiration date when planning future Continuing Reviews.

The approved consent documents are not watermarked as the UMMS IRB expects that these will be provided by the local IRB in the local language.

The IRB approved the research from 7/27/2024 to 7/27/2027 inclusive. Forty-five (45) days before 7/27/2027 or within 30 days of study close, whichever is earlier, you are to submit a completed continuing review and required attachments to request continuing approval or closure.

If continuing review approval is not granted before the expiration date of 7/27/2027, approval of this research expires on that date.

IMPORTANT: Local IRB/ethics board review must be obtained prior to initiation of any research activities.

In conducting this research, you are required to follow the requirements listed in the Investigator Manual (HRP-103), which can be found by navigating to the IRB Library within the IRB system.

Sincerely,

Crystal Davis, MPH, CIP
IRB Analyst

cc: [Deogwoon Kim](#)

Adapting effective mHealth interventions to improve uptake and adherence of the HIV pre-exposure prophylaxis (PrEP) in Thai young MSM

Study Protocol and Statistical Analysis Plan

NCT05243030

Version Date: July 18, 2024

INVESTIGATOR STUDY PLAN - REQUIRED

1. TITLE

“Adapting effective mHealth interventions to improve uptake and adherence of the HIV pre-exposure prophylaxis (PrEP) in Thai young MSM”

Version date: 5/6/24

2. EXTERNAL IRB REVIEW HISTORY*

Thai IRB approval has been completed prior to starting human subject research.

Thai IRB number: Med Chula IRB 760/64

Thai IRB Contact information: The Research Ethics Review Committee, Research Division, Faculty of Medicine, Chulalongkorn University, Ext 4493

3. PRIOR APPROVALS:

No prior approvals. No conflict of interest.

4. OBJECTIVES*

This study aims to develop and pilot a multi-component, technology-based intervention to promote both motivation to begin PrEP (“uptake”) and sustained adherence to PrEP. Our specific aims are to:

Aim 1: Adapt MESA to develop MES-PrEP and develop MTM for HIV-negative Thai YMSM. We will recruit 50 HIV negative YMSM from two HIV clinics in Bangkok, Thailand. We will also recruit 5 healthcare providers for interviews.

Aim 2: Conduct a pilot RCT to evaluate the feasibility, acceptability, and preliminary efficacy of an intervention combining MES-PrEP and MTM to increase PrEP uptake and adherence among Thai YMSM. 120 HIV negative YMSM (60 PrEP naïve and 60 PrEP users) will be recruited from two HIV clinics and followed for 6 months.

Hypothesis H1: We will be able to recruit 120 YMSM (60/clinic), and >85% will be retained in each study condition at 6-month follow-up.

Hypothesis H2: The intervention will be associated with greater PrEP uptake and adherence compared to control at 6-month follow-up. (also see proposal-specific aims Page 1)

Motivational Enhancement System for PrEP Uptake and Adherence (MES-PrEP) is a two-session, computer-delivered behavioral education intervention (iPad delivery is now available) to promote PrEP initiation and adherence among young MSM who are at-risk for HIV.

5. BACKGROUND*

Thailand has the highest adult HIV seroprevalence in Asia (1.1% in 2017).⁶ The rate of new HIV infections among MSM has dramatically increased over the past two decades.⁷ Of all new infections, 44% were among MSM.⁴¹ There were an estimated 590,700 MSM in Thailand in 2017,⁶ among whom HIV prevalence is estimated to be ~20% to nearly 30% over the past few years.⁴² Prevalence varies greatly by location. HIV prevalence among MSM in Bangkok increased from 17.3% in 2003 to 28.6% in 2015, making it the highest in Asia-Pacific region.^{4,43} In addition, HIV incidence rates among YMSM are alarmingly high: 12.2 per 100 person-years

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(PY) in Bangkok¹⁰ and 8.4 per 100 PY in Chiang Mai.⁴⁴. Given the expanding HIV epidemic among YMSM^{33,34,40}, effective interventions for YMSM are critical to the success of the UNAIDS' Fast Track Strategy: ending the AIDS epidemic by 2030.⁸

Pre-exposure prophylaxis (PrEP) is an efficacious and promising new HIV prevention strategy but uptake and adherence have been low. In this study we shall adapt and pilot test two technology-based interventions designed to motivate uptake of and sustain adherence to PrEP in HIV-negative YMSM, targeting major barriers to PrEP uptake and adherence for YMSM in Thailand. (Also see Significance A1, A2, A3, A4, proposal pages 2-3)

6. INCLUSION AND EXCLUSION CRITERIA*

Eligibility is the same for both Aim 1 and Aim 2 phases of the study.

YMSM will be eligible based upon the following **inclusion** criteria consistent with CDC and Thailand PrEP Guidelines:^{115,116} 1) age 16-25 years; 2) men who report sex with men in the past 12 months; 3) laboratory confirmed HIV negative status; 4) self-reported evidence of being at-risk for HIV acquisition, including one of the following in the past 6 months: having a sex with an HIV-positive partner, having anal sex without using a condom, being diagnosed with an STI, or having any illicit drug use (e.g., Amphetamine type stimulants); 5) able to understand, read and speak Thai; and 6) either having not started PrEP (Group 1: PrEP naive) or currently on PrEP but not adherent to PrEP (taking ≤ 3 pills/week) in the past 3 months (Group 2: PrEP users).

Exclusion criteria are 1) in a mutually monogamous relationship of > 6 months with a partner who recently tested HIV-negative; 2) a serious cognitive or psychiatric problem that would compromise ability to provide informed consent; and 3) currently enrolled in another HIV intervention study. We plan to recruit YMSM from a broad range of socioeconomic backgrounds; therefore, mobile phone ownership is not required for participation, and a mobile phone will be provided at no cost to the participants who do not have one.

- *Adults unable to consent (adults lacking capacity).* No
- *Individuals who are not yet adults (infants, children, teenagers).* Yes (16-17 years)
- *Pregnant women.* No.
- *Prisoners.* No
- *Non-English-speaking subjects.* Yes

Five providers will be recruited from our partner clinics with at least 1-year experience working with HIV-negative YMSM (i.e., PrEP prescription and counseling)

7. STUDY-WIDE NUMBER OF SUBJECTS*

N/A

8. STUDY-WIDE RECRUITMENT METHODS*

N/A

9. STUDY TIMELINES*

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This study has been approved for no-cost extension (06/01/21—05/31/2025).

Table 2: Proposed Project Timeline		
Phase	Months 1-3	Protocol development and training
I	Months 4-8	In-depth interviews and data analysis
II	Months 9-12 Months 11-15	Adapting MES-PrEP and MTM Beta-testing and refinement
III	Months 16-28 Months 29-36	Pilot RCT trial Data analysis Preparation for R01 submission

10. STUDY ENDPOINTS*

Aim 1—qualitative study to explore barriers and facilitators of PrEP uptake and adherence to inform the intervention development. (Proposal C.5, C.5.1, and C.5.2)

Aim 2—a pilot RCT to evaluate the feasibility, acceptability, and preliminary efficacy of an intervention (proposal C.7, C.7.5 and C.7.7)

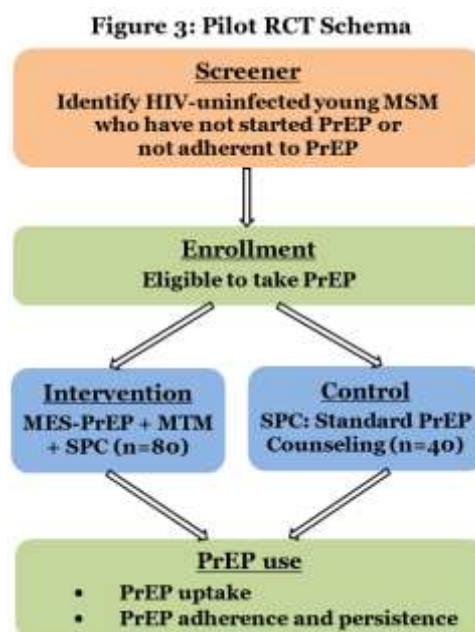
11. PROCEDURES INVOLVED*

Intervention (MES-PrEP and MTM) development and testing will be guided by the framework of the ADAPT-ITT model.¹¹⁴ This multi-phase model is designed to guide adaptation of evidence-based interventions for people with HIV or who are at risk for HIV. ADAPT-ITT begins with a needs assessment and progresses to evaluating intervention efficacy. There are 3 phases in the proposed study.

AIM 1:

For Aim 1, we will explore barriers and facilitators of PrEP initiation and adherence through (in-person) in-depth interviews with 50 HIV-negative Thai YMSM and 5 clinicians to inform intervention content and delivery. Interviews will provide rich data of barriers and facilitators to PrEP initiation and adherence among our target population. Interviews will be audiotaped, transcribed, and translated into English by a US co-investigator who is fluent in Thai. Interviews will last about 30 minutes. Once qualitative data analysis is completed, the audio recordings will be deleted. The US-Thai team will also prompt for participants' suggestions and feedback for intervention delivery captured during interviews in adapting and developing the two components of the intervention (MES-PrEP and MTM).

Using the results of the interviews, we will adapt the two components of the intervention (MES-PrEP and MTM). We have successfully used an existing MI-based intervention structure in CIAS (MESA) and rapidly adapted content (e.g., questions, knowledge



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content, response options) for other populations, health behaviors, and chronic conditions (e.g., HIV to asthma). The adaptation process will utilize a youth advisory board (YAB) of 8-10 eligible Thai YMSM to review intervention content and approaches via theater testing (see C.5.1). Following this, 10 MSM will complete one-on-one beta-testing of the interventions and provide additional feedback to guide refinement.

Data Transcription: Data obtained from audio recordings will be uploaded to the University of Massachusetts Medical School secure server. Audio data will first be translated by bilingual Thai study staff into English. It will then be transferred to a professional transcription service to generate computerized transcripts of the focus groups and interviews. Identifiers will be removed after transcriptions have been checked for accuracy by the study team. The de-identified transcript will be kept as a MS Word document where it will be saved to the UMMS server and uploaded to a qualitative research software program to be coded for analysis.

Data Storage/Security: All study data related to a given subject will use a subject ID, rather than personal identifiers. All paper copy data will be stored securely at UMass Medical School in a locked file cabinet, and all computer entered data and audio files will be stored on password-protected computers with encryption algorithms within the UMass Medical School server. No identifiable data (name, DOB) will be linked to study data (demographic or interview data). Only the study investigators and research support personnel have access to the study data, and only those directly involved in the consent and data collection process will have access to identifiable data in the consent forms. Anyone with access to data will have certification for human subject protection training.

AIM 2:

We will launch a pilot RCT to evaluate the feasibility, acceptability, and preliminary efficacy of MES-PrEP and MTM to increase PrEP uptake and adherence among Thai YMSM. We will enroll 120 YMSM (60 YMSM on PrEP and 60 PrEP-naïve YMSM) from the two HIV clinics. The 60 PrEP-naïve YMSM are those who are at high-risk and eligible for PrEP but have not decided to start PrEP. We anticipate enrollment of 20 participants per month (for 6 months). Participants will be randomized to receive MES-PrEP + MTM (intervention) vs. standard PrEP counseling (control) in a 2:1 ratio, stratified by current use of PrEP (PrEP naïve vs. PrEP users). 2:1 allocation was chosen to maximize collection of feasibility and acceptability data among intervention participants. Separate randomization for YMSM who are on PrEP and YMSM who are not starting PrEP will be computer-generated using Qualtrics. The primary outcome will be acceptability, feasibility, PrEP uptake and adherence assessed through CASI and DBS testing.

Intervention and control conditions. All participants will receive one-on-one, in-person counseling (Standard PrEP counseling) at baseline, months 1, 3 and 6 at both clinics. The intervention group will receive all three components (Figure 3). Two sessions of MES-PrEP will occur at baseline and one-month in clinic space. Research staff will give an iPad installed with MES-PrEP to a participant and assist the participant in completing the sessions. Intervention participants will receive daily text messaging between the intervention (MES-PrEP) sessions for 30 days (Month 1). Intervention participants will receive weekly text messaging thereafter until the end of Month 6, if participants opt to receive.

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Self-report measures will be administered using the cloud-based CASI in Thai at baseline, immediately post-intervention (IP) at the end of the first month and 3- and 6-months follow-up. The IP assessment will only include PrEP uptake and adherence, sexual risk, alcohol and drug use to reduce participant burden. Participants in the intervention group will complete two additional scales at the 3-month follow-up to assess their acceptability of MES-PrEP and MTM. In CASI, the participant sees each question and its response list on a private iPad screen. The response is entered by pressing a number keypad. The data are stored directly in password-protected Qualtrics. CASI elicits more valid and reliable data compared with face-to-face or written questionnaires. The topics we assess are sensitive; CASI allows greater privacy and removes barriers to honest responding. It reduces the quantity of missing data and interviewer bias. Our research team has been using Qualtrics for CASI for over 8 years.

After completing the second session of MES-PrEP, participants will be invited to an exit interview. The purpose of the interview is to learn in-depth about their experience with MES-PrEP and MTM, acceptability, ease of use, difficulties encountered, and the impact on their PrEP uptake behavior. The participants will be selected using a purposive sampling strategy based on their intervention engagement level, current PrEP use, and adherence level.

Clinicians will also draw blood samples through venipuncture (6 ml) for HIV testing, syphilis testing and Tenofovir diphosphate measurements (to measure the amount of PrEP medication in the bloodstream) at baseline, 1, 3, and 6 months. Blood samples will be collected at clinic visits and stored up to 24-hours prior to card spotting with no deterioration of sensitivity. Once cards are spotted and dried, cards are placed in plastic bags and stored with desiccant and humidity indicators at $\leq -20^{\circ}\text{C}$ at Tangerine Community Health (TCH) Clinic laboratory.¹⁰⁶ Samples will be shipped, on dry ice, to the Dr. Cressey's lab at Chiang Mai University, Thailand within two weeks. Blood samples for HIV and syphilis testing will be obtained at clinical visits. Testing and storage will follow the lab's protocols. Urine, oral, and rectal swabs will be collected for gonorrhea and chlamydia testing at baseline and 6 months. If a participant tests positive for HIV or syphilis, they will be scheduled for confirmatory testing and counseling and will receive free treatment through either clinic

12. DATA AND SPECIMEN BANKING*

N/A

13. Data Analysis and Management

Aim 1:

We will utilize a systematic, yet rapid, approach to thematic analysis to maintain rigor while adhering to the study timeline. Data gathered through interviews will be managed and coded using NVivo 10. Two members of the research team (led by Dr. MacDonell) will develop and refine codes based on a priori areas of interest and apply the codes to interview content. We will follow the guidelines process as detailed by Braun and Clarke. The first step is to become familiar with the data by reviewing the interviews, recording initial thoughts and ideas. In the second and third (iterative) steps, coders generate, define and apply initial codes through systematic review of the data set, which will result in a collation of codes within the identified broad areas. To streamline the process, analytic steps four through six will be conducted only within discussions of PrEP uptake and adherence. Coders will then finalize themes within the key interest areas (e.g., knowledge, attitudes, skills). Coding will be monitored to maintain a kappa coefficient of ≥ 0.90 . Discrepancies will be discussed and resolved by Drs. MacDonell, Rongkavilit, and Wang. *Moreover, motivational statements promoting PrEP use will be generated from each theme and the statements will be grouped by Drs. MacDonell, Rongkavilit, and Wang into one of the two text*

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message libraries, PrEP initiation and PrEP adherence libraries. The selected statements for text messaging will not contain any explicit word related to HIV, MSM or risk behaviors to avoid disclosure or breach of privacy.

Aim 2:

Dr. Wang will provide regulatory support and monitoring: site monitoring of recruitment and retention; site compliance with study procedures; and technical assistance queries and concerns. Prior to data entry, all data collection forms will be uniquely coded and de-identified. Data will be entered directly from forms and laboratory reports by site staff into an SPSS database. CIAS data are downloaded as Excel and converted to SPSS. The data management team will maintain the SPSS database, review completed data sets for completeness and legibility, and perform necessary corrections to incomplete or errant data, including querying sites and re-contacting participants if necessary. The data manager will be responsible for checking for completeness and accuracy of data entry. Data quality will be examined before statistical analysis begins, including examination of missing data, assessment of distributional assumptions, and identification of outliers. Differential attritions at all waves of follow-up will be examined. The psychometric properties of the instruments will be examined. The primary hypotheses are concerned with the effect of MES-PrEP on adherence to PrEP using a multi-method assessment approach. Visual analogue scale of adherence will be transformed and combined to form a standardized composite score (e.g., z score). (also see proposal C7.6)

Plan for statistical analysis

Evaluate the feasibility and acceptability of the intervention (MES-PrEP+MTM). We will estimate recruitment rates, overall and per condition. The difference in retention at 3- and 6-months between the intervention and control groups will be examined using chi-square test. Depending on the distribution of acceptability and satisfaction ratings, we will assess differences in levels of acceptability between the two groups using t test or the Mann-Whitney test. Point estimates for mean System Usability Scale score ≥ 50 and $>50\%$ of participants respond to at least one text message and complete at least one MES-PrEP session will be considered the minimum criteria for acceptability and feasibility.¹²⁹

Evaluation of preliminary efficacy: The intervention effect on PrEP uptake and adherence will be assessed in three steps. (1) Assess comparability of the intervention and control groups. Baseline differences between groups will be examined using chi-square test and t test. Variables that significantly differ between groups will be used as covariates in multivariate analysis. (2) Bivariate analyses. The difference in adherence to PrEP (VAS and 4-week percent taken) between groups will be examined using the Mann-Whitney test (instead of t test) as these outcomes are usually non-normally distributed. A participant will be classified as adherent if his tenofovir level in DBS reflects the use 4-7 days/week (TDF/FTC tablets) over the prior 6 weeks (almost 100% preventive effect). Participants whose tenofovir levels cannot be assessed will be classified as non-adherent. The proportion of participants in each group who are adherent to their prescribed PrEP based on DBS results and proportion of PrEP uptake at 1- 3- and 6-months will be compared using the chi-square test. (3) The intervention effect on PrEP uptake and adherence will be further assessed using mixed-effects modeling, controlling for potential confounding factors (e.g., age, and education) and possible baseline differences. To use the mixed effect modeling analysis in assessing intervention effect, an interaction term (intervention group by time) will be included together with other covariates. A significant beta coefficient of the interaction term at $p < 0.05$ level will be used as evidence supporting the intervention effect.

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Missing data will be handled using full information maximum likelihood estimation. In addition, effect sizes will be estimated for the primary outcomes. The analyses will be conducted using SAS 9.4 statistical software package. (also see proposal C7.7)

Plan for exit interview analysis: We will use the same method that we used to analyze interviews for Aim 1 (p. 5).

14. PROVISIONS TO MONITOR THE DATA TO ENSURE THE SAFETY OF SUBJECTS*

A data and safety monitoring board (DSMB) will be formed by individuals to be named. The DSMB will include at a minimum 3 members, one content-related expert and a biostatistician. There will also be a member of the DSMB with pediatric or adolescent expertise, as to provide context for those aged 16 and 17 years enrolled in the study. All of the members will be independent from any professional or financial conflict of interest with the research project and study investigators.

The Thai PI will review adverse event reports on an ongoing basis. Thai project manager will report adverse events to Thai PI every week.

15. WITHDRAWAL OF SUBJECTS WITHOUT THEIR CONSENT*

NA

16. RISKS TO SUBJECTS*

Aim 1:

Participants may feel embarrassed or discouraged answering personal questions regarding risk behaviors or disclose confidential information. However, we do not expect that the interviews, which will be done mainly through CASI in a private room, and the mobile phone-delivered MES-PrEP sessions, will be unduly stressful. Based on our prior pilot study, participants' responses to the study were unanimously positive. Participants can refuse to answer any question at any time without jeopardizing their enrollment in the study or compensation.

There is also a risk of breach of confidentiality for interviewees. To help protect personal information, we will store subjects' names separately from research data and code research data with a subject ID. We will keep paper documents under lock and key. We will keep electronic information on secure computer networks.

Aim 2:

Participants may feel embarrassed or discouraged answering personal questions regarding risk behaviors or disclose confidential information. However, we do not expect that the interviews, which will be done mainly through CASI in a private room, and the mobile phone-delivered MES-PrEP sessions, will be unduly stressful. Based on our prior pilot study, participants' responses to the study were unanimously positive. Participants can refuse to answer any question at any time without jeopardizing their enrollment in the study or compensation.

There may be physical risks associated with venipuncture. It can result in discomfort, bleeding, bruising and, rarely, infection of the puncture site. To reduce the discomfort from venipuncture,

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the procedure will be performed by experienced phlebotomists. Venipuncture may leave a mark on the skin and the participant may face a difficult question about the mark by family members, partners or peers. There is always the possibility that knowledge about participants, including being TGW or PrEP use, may be revealed to others either within or outside the project as a result of their participation. The above-mentioned potential risks will be included in the consent form.

Additionally, there are social and psychological risks associated with testing for STIs and HIV. Being tested for HIV can make you feel nervous or anxious about the test results. If other people learn about your positive test results, there might be a risk that you could be treated unfairly or badly, and even have trouble obtaining insurance or employment. To the extent permitted by law, the researchers will keep your test results confidential and will not release them to anyone without your written permission. If you test positive, you will be scheduled for confirmatory testing and counseling and will receive free treatment through either clinic.

As MES-PrEP is health behavior counseling and not a mental health treatment, supervision by a licensed mental health provider is not required. However, IHRI has a psychiatric service nearby at Chulalongkorn University Hospital and is available for emergency and non-emergency mental health management. The research staff will be educated on the recognition of important mental health symptoms that require urgent psychiatric interventions. These include intense feelings of personal distress (e.g., anxiety, depression, anger, panic), obvious changes in functioning (e.g., neglect of personal hygiene, unusual behaviors), catastrophic life events (e.g. victimization, natural disasters), and danger to self or others. The psychiatrists affiliated with the study site are also available by phone and/or pager. This information will be included in the consent form. (also see “Protection of Human Subjects”)

All participants will be reminded of the risks of disclosure if someone else sees the motivational text messages (MTM). All participants have the right to request cancellation of MTM at any time. Text messaging has already been developed and utilized successfully in an adherence intervention research among HIV-positive Thai youth using the FrontlineSMS system. Messages will be sent and received by a secure password-protected computer at the Institute of HIV Research and Innovation (IHRI). In addition, a unique password entry will also be required before the MTM can be viewed on the participant’s phone. (also see “Protection of Human Subjects”)

17. POTENTIAL DIRECT BENEFITS TO SUBJECTS*

Participants may gain better knowledge about PrEP and HIV while taking part in the study, as well as learn how to use PrEP more effectively for HIV prevention.

18. VULNERABLE POPULATIONS*

Study participants are young men who have sex with men (YMSM) aged 16-29 years. Participants ages 16-17 years will be included without parental consent. Please see section #31 for additional information.

19. MULTI-SITE RESEARCH*

This study is a collaboration between UMMS (lead investigator) and Institute for HIV Research and Innovation, Thailand.

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The two PIs and co-Is will communicate weekly by a regularly scheduled telephone conference and by additional email/telephone conversations as necessary, to discuss study design, data analysis, and all administrative responsibilities. The two PIs will work together to coordinate international travel between the United States and Thailand. The PIs will share their respective research results with each other and key personnel. They will work together to discuss any changes in the direction of the research project and the reallocating of funds, if necessary.

20. COMMUNITY-BASED PARTICIPATORY RESEARCH*

NA

21. SHARING OF RESEARCH RESULTS WITH SUBJECTS*

Making study results available to study participants after completing the study is an important step towards engaging the community. Community engagement has become an important ethical requirement for research involving human subjects, particularly marginalized populations. We will not necessarily be sharing the study results with the individuals per se. However, we propose to conduct town hall meetings at the Institute of HIV Research and Innovation (IHRI), the clinics, and Non-government Organizations in Thailand. We will also present findings to community advisory groups within IHRI.

22. SETTING

Institute of HIV Research and Innovation (IHRI), Thailand and its Pribta Clinic brings the latest scientific discoveries and practices directly to the benefit of the clients. Building trust and rapport with the clients, clinicians are able to reach and recruit the most vulnerable of all populations in to care such as men who have sex with men, transgender woman, and people who use drugs into services and research studies. Thai strong research collaborations expand from local grass roots foundations such as the Rainbow Sky Association of Thailand (RSAT), Service workers in Group foundation (SWING) and encompasses regional and international bodies such as Family Health International, United States Agency for International Development (USAID), the Armed Forces Research Institute of Medical Sciences (AFRIMS), University of Nottingham United Kingdom, Military HIV Research Program (MHRP), UCSF Weill Institute for Neurosciences, Yale University Neurological Infections and Global Neurology etc.

YMSM will be recruited from three large clinics in Bangkok, Thailand to ensure diversity in the respondent population (see Facilities). Thai Red Cross (TRC) Anonymous Clinic. TRC Anonymous Clinic has a large YMSM client population. Rainbow Sky Association of Thailand (RSAT) clinic is community-based and funded by USAID/PEPFAR with a partnership with IHRI. It has implemented the Key Population-Led Health Services (KPLHS) Model since 2015 in a highly populated area in Bangkok to provide HIV health services for key populations, including MSM. Service Workers In Group Foundation (SWING) Clinic is another community-based organization that delivers KPLHS services to key populations, particularly male sex workers, located in red-light districts of Bangkok.

23. RESOURCES AVAILABLE

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Principal Investigator (contact PI) is a Professor in the Department of Population and Quantitative Health Sciences, University of Massachusetts Medical School. His research has focused on HIV prevention, adolescent health risk behavior, and implementation of youth evidence-based interventions. He has authored over 80 peer-reviewed manuscripts including 30 on which he has served as the lead author. He is experienced in research methodology and advanced statistics. He will be responsible for overall project direction; quality assurance; data analysis and interpretation, preparation of manuscripts and research dissemination. In addition, he will ensure that the project adheres to the timeline.

- Multi-Principal Investigator (MPI) is the Executive Director at the Institute of HIV Research and Innovation (IHRI). She has extensive experience in conducting PrEP studies among Thai men who have sex with men (MSM) and transgender women (TGW). She will serve as a dual PI to oversee the conduct of all research activities including data collection and management. She will assist PI in overseeing the progress and monitoring the quality of the proposed study. She will take primary responsibility for the day-to-day management of this project at IHRI and training of Thailand staff.

Co-investigator #1 is an Associate Professor in the Department of Family Medicine and Public Health Sciences, Wayne State University School of Medicine. Her background is in developmental psychology, focusing on health disparities and adherence to illness self-management in emerging adulthood. She is experienced in the application of mobile health technologies for high-risk adolescents and young adults with HIV, including Motivational Enhancement System for Adherence (MESA). Working with the Thai team, she will be responsible for the qualitative design and analysis, and the development and implementation of the mobile phone-based text messaging and computer-delivered brief intervention in this study.

Co-Investigator #2 is a clinical Professor in the Department of Pediatrics, University of California San Francisco, Fresno Campus. He has worked in the field of pediatric and adolescent HIV medicine for nearly 20 years in Thailand and the US (mainly at WSU). He continues to maintain strong ties with IHRI which has resulted in bipartisan commitments to conduct collaborative studies with IHRI on risk behaviors in Thai youth, including Thai Healthy Choices study. He will work closely with PIs in adapting and pilot testing the two mhealth interventions targeting PrEP uptake and adherence in HIV-negative Thai young men who have sex with men.

- Co-investigator #3 is an Associate Professor in the Department of Quantitative Health Sciences, University of Massachusetts Medical School. He is a computer engineer by training. He has focused the last 10 years on developing and testing persuasive technologies for smokers. He has extensive expertise in mHealth interventions, especially text messaging-based behavioral interventions. He will work closely with PI and team in developing and programming motivational text messages to promote PrEP use among Thai young MSM.

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- Research Physician, Technical Support. He will take responsibility for the day-to-day management of this project at the Thai site, including participant enrollment, tracking and retention, study progress, troubleshooting, and coordination among site research staff (lab technicians) to ensure an effective study flow at the site. [REDACTED].
- Two consultants: Consultant #1 is a Professor of Psychology in the Department of Behavioral Sciences and Social Medicine, Florida State University College of Medicine. She will collaborate on the overall design of the proposed project. She will assist PI in the scientific, training and technical management of the project. Consultant #2 is a Professor of Pediatrics and founding dean of Hackensack Meridian School of Medicine at Seton Hall University. She will assist the PI in adapting behavioral intervention (e.g., review the content and format for appropriateness for the target age range as well as the overall educational approach) and providing necessary guidance and support to ensure successful implementation of this project. Two consultants will not have access to raw data.

The investigators at WSU and UCSF will also contact their own IRBs to determine if they need to apply for their IRB approval (once we secure UMass IRB).

24. LOCAL RECRUITMENT METHODS

Aim 1:

We will develop culturally- and developmentally-tailored marketing materials. Recruitment will be led by the Thai study staff. Materials will be placed at physical and online venues, including study clinical sites and community venues that serve MSM (e.g., health centers, bars/clubs, community organizations).

Potential participants will complete a pre-screener over the phone or in-person. Research staff will determine if the MSM meets inclusion criteria and complete informed consent. Research staff will then schedule a 30-minute appointment to complete the in-depth interview.

We will recruit 15 young MSM who have never used PrEP and 15 young MSM who have previously used PrEP.

Additionally, we will recruit 5 providers who work at the two clinic sites. Providers will be recruited by email and word of mouth.

Participants will be remunerated \$25 for their time.

Aim 2:

We will develop culturally- and developmentally-tailored marketing materials. Materials will be placed at physical and online venues, including study clinical sites and community venues that serve MSM (e.g., health centers, bars/clubs, community organizations).

Potential participants will complete a pre-screener over the phone or in-person. If eligible and interested in participating, MSM will complete an in-person screening at one of the study clinics. After providing verbal consent, they will complete a pre-baseline survey assessing basic demographic information, history of HIV/STIs and HIV testing, access to HIV/STI diagnostic and treatment services, recent sexual behavior, use of PrEP, and knowledge and acceptability of

INVESTIGATOR STUDY PLAN - REQUIRED

PrEP. They will undergo HIV testing (4th generation serum) and screening for Hepatitis B (surface antigen and antibody), Hepatitis C (antibody), and renal insufficiency (serum creatinine) to confirm eligibility for PrEP and the study. Research staff will determine if the MSM meets inclusion criteria and complete informed consent. The screening visit, enrollment and baseline assessment should occur on the same day, or failing that, within one week. After signed consent is obtained, participants will be asked to provide contact information for a family member and/or friend who can be called if they cannot be reached.

Participants will be compensated \$25 for the baseline study visit, and for each follow-up. Participants will receive a courtesy award of \$16 (THB 500) for completing the final (6-month) visit.

Participants will receive cash compensation for completing weekly survey. Each person receives \$1 (THB 30) each week the participant completes the survey. If a participant achieves a perfect response rate of 4 weeks per month, he will receive a courtesy award of \$3 (THB 100) at the end of the fourth-week survey.

25. LOCAL NUMBER OF SUBJECTS

Aim 1: 50 young men who have sex with men and 5 clinicians

Aim 2: 120 young men who have sex with men

26. CONFIDENTIALITY

Maintenance of participant confidentiality is essential. The study team will make every effort to protect the confidentiality of all participants. In addition, participants will be reminded that they have the option to skip questions and entire instruments to reduce risk of unintended self-disclosure. Safeguarding confidentiality of personal data reported in the study is maintained through the use of first names or nicknames only during the audiotaped sessions. We will use ID codes, not full names or other personal identifiable information, on all research documents, audio files, study-related electronic files and forms, and specimens. Research staff will verify that all instruments and research materials are collected before the participant leaves a research site. All study-related documents including the locator information form and the signed consent form will be kept in a locked file cabinet in a research staff's office. The master list referencing ID codes to participants' names will be kept in a locked file cabinet in a different research staff's office. The electronic case report forms and the laboratory results will be stored using the secure IHRI Electronic Data Capture program for which only research staff have access. The MTM system utilizes the FrontlineSMS system, which secures data and preserves the anonymity of study participants. All MTM activities are conducted centrally at IHRI by a trained information technologist, thus minimizing the risk of a breach in confidentiality. We will use covert language in the MTM to avoid using any explicit word related to HIV and/or MSM. The audio files and CASI database will be kept on a secure IHRI cloud-based storage network with password protection and Qualtrics data centers, respectively, to which only onsite PI, Dr. Nittaya Phanuphak will have access. A secure server is used for electronic data back-ups and is housed in a locked Information Technology office at IHRI. The master list, the locator information and all paper documents will be destroyed at the end of the study. All electronic files including audio

INVESTIGATOR STUDY PLAN - REQUIRED

files, CASI files, study-related electronic files and forms, and the back-up files will be deleted after the completion of data analysis. Data analysis will be done only in aggregate. No individually identifiable information from the data collected will be published. (also see Protection of Human Subjects—“Protection Against Risks”).

27. PROVISIONS TO PROTECT THE PRIVACY INTERESTS OF SUBJECTS

Confidentiality will be fully kept when contacting the participant. During the consent process, a research team member will invite youth to participate, describing what would be involved, that the information would be confidential and that they would not need to participate and that their physicians will not know the research status of any individual youth. Youth’s questionnaires are confidential.

28. COMPENSATION FOR RESEARCH-RELATED INJURY

There are no anticipated physical risks of this study.

29. ECONOMIC BURDEN TO SUBJECTS

There is no economic burden to subjects.

30. CONSENT PROCESS

Aim 1:

Potential participants will complete a pre-screener over the phone or in-person. If eligible and interested in participating, MSM will complete an in-person screening at one of the study clinics. After providing verbal consent, research staff will determine if the MSM meets inclusion criteria and complete a written informed consent. The in-depth interview will then be scheduled and/or completed during that visit.

Aim 2:

Potential participants will complete a pre-screener over the phone or in-person. If eligible and interested in participating, MSM will complete an in-person screening at one of the study clinics. After providing verbal consent, research staff will determine if the MSM meets inclusion criteria and complete a written informed consent. The screening visit, enrollment and baseline assessment should occur on the same day, or failing that, within one week.

31. PROCESS TO DOCUMENT CONSENT IN WRITING

A written consent will be obtained for both Aim 1 and Aim 2 portions of the study. In the 1st quarter of Year 1, all members of the Research Team will join in a 1.5 day-long training workshop about roles, responsibilities, data flow, ethical issues (consenting) and practice with the forms. A one-day refresher training will be conducted in subsequent years for new and existing personnel.

According to CDC and Thailand PrEP Guidelines, TGW is an important target population for PrEP intervention. We choose to study 16-29-year old Thai TGW because of 1) very high levels of sexual risk behaviors; and 2) high rates of HIV/STI infections in TGW. The age of participant consent without the requirement of parental or legal guardian’s permission in Thailand is 18

INVESTIGATOR STUDY PLAN - REQUIRED

years or older. However, we believe that the protection of subject confidentiality related to HIV and risk behaviors is of utmost importance in this study. Requiring those aged 16 and 17 years to disclose their HIV status and/or risk behaviors to their parents or guardians may put them at risk of social, financial, or physical harm and impair relationships. Therefore, we believe it is important to allow participants under 18 years to give and sign consent without parental or guardian permission. For this same reason, the IRB allowed those under 18 to sign and give consent without parental or guardian permission in our previous pilot R34 study. The research study, including questionnaires, venipuncture, STI testing, and mobile interventions, pose minimal risk to subjects. We will require one member of the DSMB to have pediatric or adolescent expertise to protect children who participate as subjects and prevent harm.

32. DRUGS OR DEVICES

NA

INVESTIGATOR STUDY PLAN - REQUIRED

eIRB Section 7.0 Attachments Upload Checklist

Follow [How to Manage Files in eIRB](#) and upload the following items as applicable to your submission. This checklist is provided for your convenience and is not a requirement for review.

	Investigator Study Plan (x)
	Sponsor protocol (no)
	Research portion of the grant (proposal)
	Human subjects portion of the grant (x)
	Written approvals from <u>ancillary reviews</u> (Clinical Engineering, COI, IBC, PRC, RSC, Students as Subjects, etc.) (no)
	Recruitment materials such as flyers, brochures, posters, scripts of radio ads, etc. (no)
	Data collection sheets, case report forms, etc. (no)
	Surveys, measures, instruments, etc. (yes)
	Measures to assess capacity to consent
	DMC or DSMB charter (no)
	Data safety monitoring plan (yes)
	Adverse event log (Yes)
	Investigator brochure or package insert for drugs (no)
	Instructions for use or approved FDA labeling for devices (no)
	Sponsor justification or FDA documentation for non-significant risk device study (no)
	IND or IDE documentation (no)
	Patient information sheet for Humanitarian Use Device (no)
	Approval order for Humanitarian Use Device (no)
	Product labeling for Humanitarian Use Device (no)
	HIPAA waiver (no)
	HIPAA authorization (no)
	Authorization to contact form (no)
	Consent form(s) (Yes)
	Assent forms(s)
	Fact sheet(s)
	Multi-site communication plan (no, ministry of education and ministry of health)
	Study staff training plan (research team members were trained for previous projects)
	SOPs or Manuals of Operations (no)
	Screening log (no)
	Compensation log (no)
	Certificates of translation or translator attestations (no)
	Data use agreements, memoranda of understanding, (no)
	Documentation of data/specimen anonymity (i.e., provider will never break the code) (no, anonymous data collection)