Buddhist Understanding and Reduction of Myanmar Experiences of HIV Stigma and Exclusion (BURMESE)

NCT05126225

Study Protocol including Statistical Analysis Plan

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3.5 APPROACH

3.5.1 Setting: The local hospital of the Community Hospital Sanpatong District (CHSD), situated in Sanpatong district, ChiangMai province, Thailand, will be the study recruitment site. The CHSD is one of the most accessed public hospitals in northern Thailand and is considered the premier hospital for HIV/AIDS treatment at the community level. The CHSD hosts clinical trial research staff for HIV medication trials and for other HIV-related social and behavioral research. It has initiated task-shifting HIV service from primary healthcare physicians to trained nurses. There are more than 5,000 individuals living with HIV currently under care at CHSD and 80% of them are currently receiving antiretroviral therapy (ART). The Community Advisory Board (CAB) and Scientific Advisory Board (SAB) will regularly review the progress of the clinical trial. Both the CAB and SAB members will receive a small honorarium for their participation.

3.5.2 Recruitment: Potential PLWH participants will be identified with assistance from the healthcare providers (HCP) at Sanpatong Hospital. The HCP will identify potential participants from among clients visiting their HIV clinics. An information sheet explaining the study will be disseminated to all PLWH clients who meet the eligibility criteria. PLWH clients will be approached by a healthcare provider to determine their interest in the study. If a client is interested, the HCP will refer them to the project staff, who will describe the purpose and procedures of the study to them. Consenting participants will be asked to complete their interviews at Sanpatong Hospital after their appointment with their providers or at another convenient time. The focus group participants with stakeholders will be identified and invited by the site study team with assistance from the administrators of Sanpatong Hospital and the local public health office. When at least 5 members are found for each group, our research staff will then schedule the time and place for when each group will meet. All potential participants for both phases of the study will be reassured that their participation is completely voluntary. Upon completion of study activities, all participants will be compensated for their time. All potential participants will be reassured that their participation is completely voluntary. Upon completion of study activities, all participants will be compensated for their time.

3.5.3 Inclusion and Exclusion Criteria: We will recruit Thai PLWH who are interested in participating in this study with the following inclusion and exclusion criteria. Inclusion criteria: Participants must (a) be at least 18 years of age, (b) be self-identifying as PLWH, (c) be able to give informed consent to the study, and (e) be physically well enough to attend counseling sessions and follow-up visits. For focus group participants, they will need to (a) serving to PLWH population, and (b) willing to share their experiences with study team personnel. Exclusion criteria: Participants who (a) have a significant condition, such as neurological or cardiovascular diseases, that prevents them from fully participating the study, or (b) are unable to communicate.

3.5.4 Procedures to Address Research Aims

3.5.4.1 **Aim 1: We aim to conduct in-depth interviews with 30 Thai PLWH and two focus group (*n*=12) with stakeholders to inform our adaptation of an evidence-based intervention for family-informed self-management.** In order to collect sufficiently diverse experiences of HIV stigma, we aim to recruit 10 women, 15 men, and 5 transgender individuals. Among the men, at least 8 will be MSM. Among the 30 PLWH, at least 8 will be sex workers, and 8 of them will be substance users. Gender, sexuality, and substance use may overlap and intersect with each other. For two focus groups of stakeholders, we aim to recruit healthcare providers (*n*=6), peer support/community leaders (*n*=4), family members and friends (*n*=2), if necessary. Two Thai-speaking researchers will conduct individual qualitative interviews in secure environments at the site offices or another participant-chosen location. Interviews will be audio-recorded with consent; however, no identifying information will be collected. The researchers will follow a semi-structured interview guide to understand participants' complex lived experiences with HIV stigma, including: (a) how they experience and feel about their lives with HIV, (b) how they experience, understand, and interpret HIV stigma, and (c) how they reduce their HIV stigma, all in the context of Buddhist-Thai culture. Questions will include: *How have you experienced changes in your life following your HIV diagnosis? How have you experienced negative events in your social relationships in relation to your HIV status, if so, what was that like? Have the events changed you regarding how you see yourself, your relationships, and the nature of human experience? What did you do to manage the negative events, as well as your responses? How might Buddhist teaching have influenced your thinking and feelings about your HIV status and negative events you have experienced? How do you think that*

being a woman/gender and sexual minority/substance user may have influenced your experience of HIV and those negative events?

To explore how community stakeholders perceive the stigma PLWH may have experienced, two researchers will facilitate the focus group discussions via face-to-face or Zoom meeting, considering the current pandemic, with participants recruited from Sanpatong Hospital. The focus groups will follow a flexible discussion guide that allows the researchers to understand participants' personal experiences or observations of the PLWH's stigma. The focus groups will further solicit their opinions about how healthcare services could help PLWH to better respond to the challenges they face.

Questions will include: *How long have you worked with the Sanpatong Hospital? Please describe your observations about the stigma that PLWH faced due to their serostatus? What are the needs of PLWH due to these unfair treatments? What challenges has you faced in trying to meet the needs of PLWH? How have the hospital staff assisted the PLWH currently? How have the services managed the stigma experienced by the PLWH? What else can be done to better meet the needs of PLWH?*

3.5.4.1.1 *Analysis of Qualitative Data*

We will use the Interpretive Description qualitative analysis approach,[127-129] guided by our working conceptual model, to analyze 30 in-depth interviews with Thai PLWH and 2 focus groups with stakeholders. We will apply procedures successfully employed in our previous mixed-method projects in which we collected and analyzed qualitative data to identify HIV stigma experiences among Myanmar PLWH. The notes and audio-recordings will be transcribed verbatim in Thai. We also follow the recommendations by Squires on cross-language qualitative studies.[130] The first 10 transcriptions will be translated into English for analysis. These transcripts will be independently translated by two individuals to confirm accuracy. Two English-speaking researchers and two Thai-speaking researchers will independently review and carefully read the transcriptions to identify and code salient concepts and categorize them into more abstract themes, with the goal of developing a coding schema.[131] Then the four researchers will meet to discuss their codes and corresponding meanings and compare their coding schemas. The researchers will resolve any discrepancies in their interpretation of the transcriptions and their organization of concepts through prolonged discussion. After reaching consensus on the coding schema, the two Thai-speaking researchers will finish coding the remaining transcriptions from in-depth interviews. To revise the model using qualitative data, we will map the results of this bottom-up coding approach onto our conceptual model and identify potential discrepancies between the data and the model. In places where the model significantly departs from the data, we will revise the model to accommodate additional constructs emerging from the lived experiences of Thai PLWH. Because our working conceptual model includes general HIV stigma and cultural factors that impact Thai PLWH, we will specifically identify both unique and common HIV stigma due to the intersecting minority identities in the local Buddhist-Thai culture, namely women, MSM, transgender, sex workers, and substance users, through constantly comparing the HIV stigma they have faced as well as their cultural meaning they assign to stigma across different groups. We will use the commercial software package Atlas.ti 8 to manage the analytic processing of qualitative data.[132] Finally, to assess the credibility of the data and trustworthiness of the findings,[133-135] we will present the summary and interpretations of the qualitative data analysis and revised conceptual model to the CAB and SAB for input.

3.5.4.1.2 *Cultural Adaptation of the Stigma Reduction Intervention Using the Revised Model*

To culturally adapt the intervention developed by the PI and colleagues, we will apply a modified ADAPT-ITT model. The original ADAPT-ITT has eight sequential steps,[136-138] including assessment, decisions, adaptation, production, topic experts, integration, training, and testing. In our modified approach, the first two steps (assessing the needs of the target populations and making decisions about which interventions should be selected for adaptation) will be skipped as the tasks in these two steps will be completed before adaptation. Therefore, we will focus on the next five steps of adaptation as summarized in **Table 2** below (the titles represent the steps), while leaving the last step of adaptation, testing, to Aim 2 of the study.

Table 2: Activities in the Cultural Adaptation of the Intervention for Stigma Reduction

Adaptation: In the original ADAPT-ITT model, the evidence-based intervention is presented to groups of PLWH in theatrical formats to gather information about which components should be changed to fit the local culture. In our modified approach, however, **we will use our revised conceptual model from AIM 1 to guide our initial adaptation**. During the adaptation, we will identify the theoretical constructs that are in the revised conceptual model but are inconsistent with the original intervention. We will create additional intervention components to be included in the treatment, in particular those inspired by the HIV stigma process among Thai PLWH in the context of Buddhist-Thai cultural beliefs and practices. For example, how sexuality and substances associated

with HIV are perceived and discussed in the local community, as well as how they impact familial relationships. After the initial adaptation, the first draft of the adapted intervention will be presented to stakeholders, Thai PLWH and if needed, their family members and friends. All the discussion sessions will be audiotaped. The participating stakeholders will also fill out a brief survey containing closed- and open-ended questions regarding the cultural appropriateness of intervention components.
Production: The data collected from the adaptation procedure will be further used to guide the production of the second draft of the intervention. In this step, an adaptation plan will be created in which all the information will be considered simultaneously and evaluated on the basis of its theoretical and therapeutic importance. In this step, **we will seek to achieve a balance among fidelity to the core elements and internal logic of the original intervention, the revised conceptual model of family-informed self-management among Thai PLWH, and the results of the focus groups**. The core elements refer to the features of the original intervention that are thought to be responsible for its effectiveness. The product is the second draft of the adapted intervention.
Topic Experts: The second draft of the intervention will be sent to selected topic experts for review. These topic experts include the local healthcare and psychosocial service providers identified by the Sanpatong Hospital staff members and the research team. These experts may include, but are not limited to, physicians, nurses, social workers, and other scholars with the required expertise in HIV care, who are also familiar with the local Buddhist-Thai cultural practices. Written and oral feedback will be solicited from these experts. The experts will, in particular, focus on validating the cultural appropriateness of the intervention and resolving potential conflicts among the core components of the original intervention, the revised affective processing model, and results of focus groups.
Integration: Feedback from the topic experts will be further integrated to generate the third draft of the intervention.
Training: After the completion of the third draft of the intervention, the PI (Dr. Chen), a Co-I (Dr. Shiu), and a clinical psychologist (Dr. Yang) will host a week-long training workshop on site. The purpose of this workshop is to train staff at Sanpatong Hospital to be interventionists for the project. The workshop will review fundamental behavioral intervention skills as well as the content of the adapted intervention. Role-play and other instructional methods will be used to develop the skills and mastery necessary to successfully deliver the intervention. The study team will also train research administrative staff to support the operation of the study.
Testing: We will test the ***feasibility***, ***acceptability***, and ***preliminary efficacy*** of the adapted intervention in Aim 2.

3.5.4.2 **Aim 2**: **To test the feasibility, acceptability, and preliminary efficacy of the adapted intervention for stigma reduction, we will employ a randomized-controlled design in which we will randomize 80 Thai PLWH to two groups and follow them for 10 weeks.**

3.5.4.2.1 Treatment group assignment: We propose to recruit 80 Thai PLWH who will be randomly assigned to either the Enhanced Treatment group (**ET**; *N*=40) or the Treatment-as-Usual group (**TAU**; *N*=40). While the ET group participants will receive the proposed stigma reduction intervention, the TAU group participants will receive typical services available in the Sanpatong Hospital that are also available to the participants in the ET group, including care co-ordination and linkage to public health nurses in local communities. Using a computer program, we will generate a list of random numbers to assign participants to either group. Numbered envelopes indicating condition assignment will be prepared and sealed. However, to ensure equivalence of gender/sexuality/substance use composition between study arms, we will stratify the sample and randomize each gender/sexuality/substance use category separately, so that each arm will consist of 40 participants with balanced gender/sexuality/substance use compositions. This balanced composition between groups will guarantee sufficient sample sizes for key subpopulations and, hence, enable subsequent analyses for possible heterogeneity of treatment effects. See **Table 3** for the sample allocation for both the ET and TAU groups. Study staff will not be aware of the assignment until the envelope is opened and the baseline survey has been performed.

Table 3: Sample Allocation for ET and TAU Groups (# in ET/ # in TAU)

Cisgender Straight Men	Cisgender Straight Women	MSM	Transgender	Substance User
8/8	8/8	10/10	5/5	9/9

3.5.4.2.2 Implementation: **The stigma reduction intervention will consist of four group counseling sessions** delivered by trained interventionists. In each session, a designated interventionist will meet with participants for 120 minutes in a designated room at the Sanpatong Hospital. To help build rapport among the group members, we will host, in total, 5 groups, including 1 group for cisgender straight men who are non-substance users (n = 8), 1 group for cisgender straight women who are non-substance users (n = 8), 1 group for MSM who are non-substance users (n = 10), 1 group for transgender individuals who are non-substance

users (n = 5), and 1 group for substance users (n = 9). The interventionist will follow the intervention manual to deliver the intervention and assign homework for group members to practice on their own. In the following sessions, the interventionist will review progress with participants, guide participants through exercises, and identify additional problems to be addressed in subsequent sessions.

3.5.4.2.3 Fidelity check: To ensure intervention fidelity, all the intervention sessions will be audio-recorded and interventionists' progress notes will be reviewed for supervision purposes; in addition, subsequent analysis of interventionists' reliability will be conducted. At the end of each month, the Thai-speaking researchers and the team will randomly select and review 20% of the recordings and progress notes throughout the study period. The research staff will host biweekly supervision sessions for the interventionists to discuss difficult cases, including their intervention decisions. Finally, the PIs (Dr. Chen and Shiu) will travel to the study site at least twice a year to provide oversight to the research personnel. The PIs will also be available daily through online communication with the research personnel for immediate troubleshooting to ensure smooth research operations. Drs. Chen, Detels, and Shiu will meet regularly and frequently online to review progress, solve emerging issues during project operations, and revise the plans for action.

3.5.4.2.4 To minimize attrition, we will implement specific procedures beginning at baseline. The procedures, which we successfully employed in prior projects, include verifying contact information at each assessment, obtaining any potential upcoming changes in addresses every month, using potential friend and family locators, collecting email addresses, and sending cards when approaching follow-up dates. Based on our prior experiences, we expect that attrition will be lower than 15% with application of these procedures. Therefore, we aim to recruit 80/(1-0.15) = 94 participants at our baseline, which after attrition may result in a sample of 80 for analysis.

3.5.4.2.5 Measurement plans: As in our ongoing studies, structured instruments (see **Table 4**) will be used to assess Thai PLWH regarding their demographics, key clinical characteristics, and psychosocial factors addressed in the intervention, including stigma, attribution styles, physical and emotional arousals, karma beliefs, insights on sufferings, mindfulness, compassion, social support, and care engagement. The psychometric properties have been established for most of the instruments among Asian populations, in particular, in our ongoing R21 project. The survey will be available in the Thai language. The survey will have 250 items in total; however, there are multiple skip patterns. Depending on the responses of Thai PLWH, the survey may have as few as 160 items. These self-report measures will be conducted via Audio Computer-Assisted Self-Interview (ACASI) and will typically be completed within 30-40 minutes. Use of ACASI lessens the likelihood of socially desirable answers and minimizes data entry errors. Similar ACASI survey programs have proven successful in studies of participants with little or no prior computer experience in Asian populations.[139] Regarding care engagement measures, many studies have used single items to measure ART adherence, for example, gathering categorical data (*yes* or *no*) to measure whether patients achieved 95% adherence. However, in this project, we will create a latent variable for all these items to further control potential measurement errors.[106,140-142] Viral load (VL) also be collected as an objective measure for adherence. The research staff in charge of data collection will be completely blind to treatment assignments of participants. Please note, our primary outcome is internal stigma, while our secondary outcomes are the indicators for care engagement, including self-reported adherence, viral load, self-reported patient engagement, and clinic visits.

Table 4: Measuring Instruments

Instrument	Items	Instrument description	Cronbach α
Demographics and clinical outcomes	15	Participants are asked about their age, gender, race, ethnicity, education, income, health insurance, possible HIV transmission route, when they first learned of their HIV diagnosis, opportunistic infections and ART-taking status, morbidity, VL, and current CD4.	
Universal Cognitive-Behavioral components of HIV Stigma			
HIV stigma (external and internal)	10 16	The HIV-serostatus subscale of the Multiple Discrimination Scale[30] will be used to measure external HIV stigma. Participants will report whether they experienced 10 different discrimination events in the past year for each of the three discrimination types, including violence, institutional discrimination, and interpersonal discrimination (*Yes*: 1, and *No*:0). A summary score will sum across the 10 items. The personalized stigma and negative image subscales of the HIV Stigma Scale[31,32,100] will be used to measure internal stigma, The scales ask participants to rank to what extent they agree with 16 statements about HIV stigma in	0.85 > 0.90

		relation to their personhood and self-image (*strongly disagree*:0 to *strong agree*: 3). A summary score will be computed to sum across the 16 items.	
Attributions	48	Attribution Style Questionnaire [143-145] is a classic measurement to assess individuals' attribution style. This assessment lists 12 good or bad outcomes and probes participants with 4 questions regarding the internality, stability, and globality of these events.	> 0.70
Emotional & physical Reactions	47	The Trait Physiological Hyperarousal Scale[146] & Dissociation and Arousal subscales of Acute Stress Disorder Scale[147,148] will be used to measure participants' perceptions of bodily activation and acute stress reactions (*very slightly* or *not at all*: 1 to *extremely*: 5) during stressful events.	> 0.85
Buddhist Philosophy and Practice			
Karma belief	4	The Fatalistic Karma subscale of the Buddhist COPE Scale[33] will measure participants' karma belief regarding to what extent they agree that they believe their actions have consequences for themselves and others and that the consequences will occur no matter what they do (*strongly disagree*:0 to *strongly agree*: 3)..	0.70
Insights on suffering	52	The Self-Other Four Immeasurable Scale[34] & Nonattachment Scale[149] will be used to measure participants' insights on suffering through capturing their sense of self, others and their insights into the constructed and impermanent nature of mental representations.	> 0.80
Mindfulness	9	The Cognitive and Affective Mindfulness Scale-Revised[35,36] will be used to measure participants' mindfulness practice, including attention, awareness, and acceptance, in their daily lives. (*Rarely*/*Not at all*: 1 to *Almost always*: 4) [101]	> 0.75
Compassion	26	The Self-Compassion Scale[37,38] will be used to measure participants' kindness toward themselves during failure, perceiving one's experiences as part of the larger human experience, and holding painful thoughts and feelings in mindful awareness.	> .85
Care Engagement			
HIV medication Adherence	6	Participants will be presented with a list of current ART medications and questions to record their history of taking or stopping antiretroviral medication. The instrument will record their current ART regimen and reasons they stopped taking ART medications, where appropriate. Note that viral load will also be used as an objective measure of adherence.	0.96
3-day recall of ART adherence	1	This one-item visual analog scale is based on [150] a 3-day adherence assessment. It accesses 3-day adherence along a continuum of "none of my doses" to "every one of my doses."	
30-day recall of ART adherence	1	This one-item visual analog scale[150] assesses 30-day adherence, reported separately for each drug, along a continuum of "none of the doses" to "every dose." This scale has been shown to correlate with other adherence measures such as MEMS caps.	
Care Engagement	13	The Patient Activation Measure – Short Form will be used to measure participants' engagement in their care, as assessed by their agreement with statements about their beliefs in their active roles in care, confidence and knowledge to take action, capacity in taking action, and staying the course under stress. (*Strong disagree*: 1 to *Strongly agree*: 5)	0.88
Clinic Visits	2	How many missed visits over the past month? How many delayed visits over the past month?	

3.5.4.2.6 Timeline: The timeline for intervention sessions and data collection is summarized in **Table 5**. There are four data collection points: Week 1 (before intervention for enhanced treatment (ET) group), Week 4 (right after intervention for the ET group), Week 7, and Week 10. Therefore, in this data collection schedule, the ET group will have one-baseline (Week 1), one post-intervention evaluation (Week 4), and two follow-ups with 3-week intervals (Week 7 and Week 10). Assessment consists of a survey and a dried blood spot test at Weeks 1 and 4.

Table 5: Data Collecting Time Points

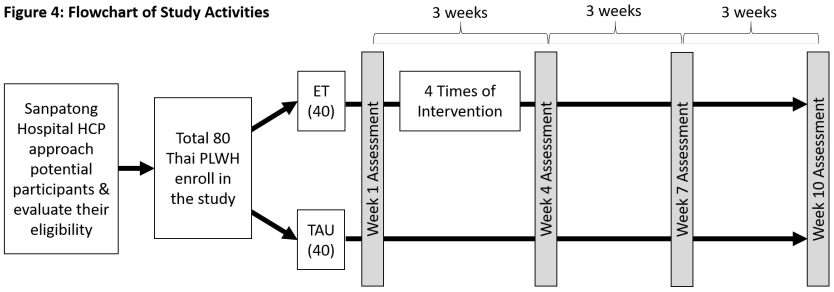
Time Points	Week 1	Week 2	Week 3	Week 4	Week 7	Week 8	Week 9	Week 10
ET Group	Intervention	Intervention	Intervention	Intervention				
	SV, VL			SV, VL	SV, VL			SV, VL
TAU Group								
	SV, VL			SV, VL	SV, VL			SV, VL

Note: **ET** = Enhanced Treatment; **TAU** = Treatment-as-Usual; SV = Survey; and VL = Viral Load.

3.5.4.2.7 A summary flowchart of the randomized waitlist-controlled trial

A flowchart is presented in **Figure 4** to summarize recruitment, enrollment, randomization, intervention delivery, and assessments. Please note that, for the ET group, the Week 1 assessment occurs right before the first intervention session, and the Week 4 assessment occurs right after the fourth intervention. In contrast, for the TAU group, there is no additional stigma reduction intervention, but the group will be assessed at Weeks 1, 4, 7, and 10. The same 3-week intervals will enable direct comparisons across conditions and assessments.

Figure 4: Flowchart of Study Activities



3.5.4.2.8 STATISTICAL ANALYSIS PLAN

3.5.4.2.8.1 To evaluate feasibility and acceptability: **To evaluate feasibility**, defined as the participation rate among eligible Thai PLWH**,** we will carefully document in study logs the numbers of Thai PLWH who are eligible to participate, approached by staff, willing to participate, and eventually enrolled in the study. **We will assess acceptability**, defined as the study completion rate, with detailed documentation of their attendance in intervention sessions, and program completion or termination. We will record their reasons for non-participation and early termination. The numbers of prompts and reminders needed to ensure participation will also be recorded. To further shed light on factors contributing to intervention acceptability, we will triangulate the study logs with an extensive structured post-intervention *exit interview*, which will probe participants about their opinions on different aspects of the adapted intervention, including relevance, delivery, and satisfaction with the activities and materials. At the end of the exit interview, any improvements that participants suggest to enhance the efficacy of the intervention in helping Thai PLWH more effectively manage their family relations and illness will be documented and implemented. All the exit interviews (*N*=40) will also be audio-recorded and transcribed. Standard qualitative coding and theme-extracting approaches as described in Section 3.5.4.1.1 will be applied to identify areas for further improvement. Finally, the interventionists will keep detailed progress notes for each session, documenting which topics and activities were covered in the sessions as well as Thai PLWH's patterns of participation. These progress notes will be triangulated with transcriptions of intervention session audio-recordings and with the exit interviews to identify active intervention components and assess their acceptability. Participants' health outcomes as a result of the stigma reduction intervention, along with their responses regarding its feasibility and acceptability, will allow us to better understand ways to assist Thai PLWH in managing their relationships and their HIV, improving their well-being, and contributing to overall health and containment of the HIV epidemic.

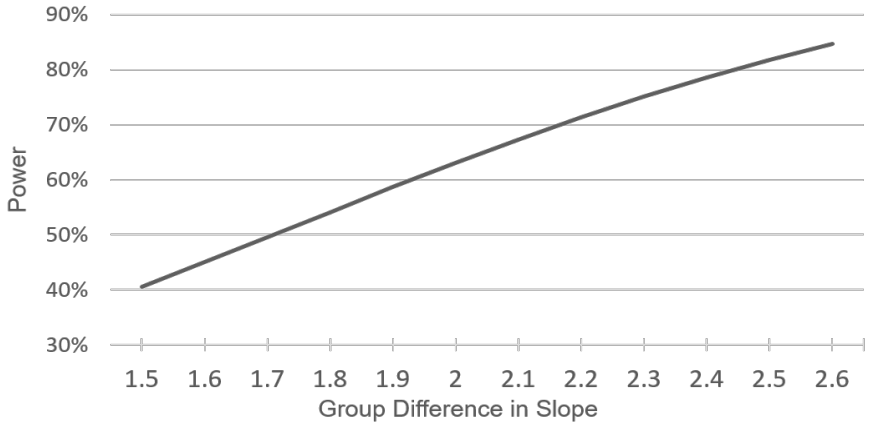
3.5.4.2.8.2 To evaluate preliminary efficacy: Our study design involves a two-group randomized-controlled clinical trial with four assessments for each participant and a total of 320 observations. **The study is not fully powered for efficacy, limiting the sophistication of the analyses we can conduct to test efficacy**. However, to obtain robust estimations, we will take the following steps: (a) we will examine the scope and mechanisms for missing data and attrition to investigate the extent to which the missing-at-random (MAR) assumption is violated, and, if it is violated, we will adapt procedures recommended by Barnes et al.;[151] (b) we will examine all measures at each observation time using univariate statistics to identify potential irregular response patterns and determine overall quality of data; (c) we will assess scale reliability and compare it to published psychometrics in comparable populations; (d) we will triangulate objective and self-report measurement of adherence; (e) we will give special attention to our key primary outcome variables (quality of life and objective health measures) as well as secondary outcome variables (stigma, disclosure preparedness, family relations, family support, self-management efficacy, adherence, depressive and anxiety symptoms, and physical symptoms; note that all the outcomes are continuous); and (f) we will investigate the quality of random assignment by conducting a series of bivariate statistics comparing selected demographic, clinical, and psychosocial factors between treatment groups at baseline. Important findings may result in the modification of subsequent analyses.

We will use Generalized Estimating Equations (GEE) to test the proposed hypotheses while controlling for stratification and basic demographic backgrounds. This GEE framework allows us to carry out statistical tests for all the major hypotheses by comparing "population averages" between groups while appropriately adjusting for autocorrelations in observations due to repeated measures for the same groups of participants. We will further apply the small-sample estimator of variance to accommodate our sample size.[152] To compute

standard errors and confidence intervals for statistical inferences, we will use a clustered sandwich estimator to obtain robust estimations. Note that, for simplicity of the exposition, controlling variables are not shown in the equations. All the statistical testing will be analyzed with the statistical software packages Stata and R. **Please note, our interpretations will focus on the size of the between-group effect and its replication in the DT group because this study is not designed to have power to detect small effects.**

We will fit the following GEE intent-to-treat model with the Thai PLWH: $g\big(E(Y_{it})\big) = \beta_{01} + \beta_{02} * Week_{i4} + \beta_{03} * Week_{i7} + \beta_{04} * Week_{i10} + \beta_{05} * I(ET_i) + \beta_{06} * I(ET_i) * Week_{i4} + \beta_{07} * I(ET_i) * Week_{i7} + \beta_{08} * I(ET_i) * Week_{i10}$ where *g(.)* denotes a proper link function; Y_{it} denotes primary or secondary outcomes in separate models for participant *i* at Week *t*; *t* = 1, 4, 7, and 10; and $I(ET_i)$ denotes a binary variable indicating whether participant *i* belongs to the immediate treatment group. In this model, β_{01} represents the mean outcome levels for DT at Week 1; β_{02}represents the slope for TAU between Week 1 and Week 4; β_{03} represents the slope for DT between Week 1 and Week 7; β_{04} represents the slope for TAU between Week 1 and Week 10; β_{05} represents the average group difference in outcomes between TAU and ET groups at Week 1; β_{06} represents the average group difference in the slope between TAU and ET groups between Week 1 and Week 4; β_{07} represents the average group difference in the slope between TAU and ET groups between Week 1 and Week 7; and β_{08} represents the average group difference in the slope between TAU and ET groups between Week 1 and Week 10. We define that the main between-group treatment effect is equal to β_{06}; therefore, we expect that β_{06}will be significantly different from 0.

Figure 5: Power Estimation with N = 80 and 4 Time Points



3.5.4.2.8.3 Sample Size Considerations**:** As the goal of qualitative components is to explore a range of experiences among Thai PLWH's experiences in family relations and self-management, as well as their opinions regarding acceptability of the adapted intervention, it is critical to include participants with a wide enough range of experiences to reach conceptual saturation. Although "saturation" and "*a priori* determined sample size" have stimulated debates in the literature,[153-155] it is generally agreed that a sample size of 30 participants should be sufficient to capture a range of experiences.[154] Therefore, the 30 in-depth interviews we utilize in our AIM 1 to revise the conceptual model, as well as the 40 exit interviews we will conduct in our AIM 2 to evaluate acceptability of the intervention, should provide sufficient saturation and guide future intervention revisions. Please note, we do not intend to fully power the quantitative data to formally test the model in this project. Rather, we will focus on the magnitude and valence of the treatment effect as well as its overall pattern during replication. However, in order to understand the size of the difference in slopes (β_{06}) between treatment groups our data can detect given our sample size, observation time points and the GEE model, we used the *liu.liang.linear,power* function in the *longpower* package[156] in the R statistical software and supplied with the preliminary data from our ongoing R21 project. The results are illustrated in **Figure 5.** Given our study designs with N = 80 and model choice (GEE), we can detect as small as 2.4 in β_{06} with 80% power.

3.5.4.3 **Aim 3**: **To revise and finalize the study protocols using results from AIM 1 and AIM2.**
The study protocols have two parts, including intervention protocol and operational protocol. The intervention protocol is the intervention manual providing a detailed, step-by-step guide for each of the intervention sessions. The goals, topics, intervention approaches, and timeframe for each module will be clearly delineated. We will use the study results from AIM 2— the feasibility, acceptability, and effect sizes—to finalize the intervention protocol. Since our intervention will be adapted using the qualitative data from our prior studies with additional input from stakeholders, we expect most intervention components will be feasible and acceptable to our participants; yet, by using the qualitative data from exit interviews and study logs, we will identify specific intervention components in need of revision, and particularly those clearly not acceptable to Thai PLWH. To further increase feasibility and acceptability of the intervention, we will recommend additional

adjustments to the intervention and submit them to the CAB and SAB for final review. We will calculate power and required sample size of the future R01 study using the preliminary effect sizes from the current project.

The operation protocol, in contrast, will address a series of necessary activities for the success of the subsequent R01 study. We will adapt an existing operation protocol from a similar project conducted by the PI in her K award as described in Section 3.3.2. In that project, the PI and the research team developed an operation protocol and successfully set up a preliminary randomized controlled trial to test efficacy of a family-centered self-management intervention for Chinese women living with HIV in China. The operation protocol will include topics such as project set-up, required facilities, inclusion and exclusion criteria, participation recruitment and retention, random assignment procedures, training materials and supervision, intervention fidelity, data collection and storage, data quality assurance, arrangement of clinical referrals for participants with mental illness, reporting of potential harm to others or themselves, timeline and important dates, and tasks and duties for personnel, among others. To refine our operation protocol so that it can cover as many diverse conditions as possible, **we will further collect data from all stages of the research implementation and keep detailed logs of all the study activities.** In this documentation, study staff will be instructed to detail not only what has happened according to the study plans but also unexpected situations that may facilitate or impede the designed activities. During regular supervision with Drs. Moolphate, Chen, Detels, and Shiu, this documentation will be reviewed and discussed thoroughly within the team members. Special attention will be given to participant recruitment and retention, and we will enlist several strategies to handle different situations and to engage participants. The feasibility data from the recruitment and retention study logs will be analyzed to identify barriers for Thai PLWH to partake and be retained in the study. Solutions to these potentially emerging problems will be brainstormed and implemented to test their effectiveness. The study team will also review related literature to identify best practices. Indeed, we previously published a study on building cross-cultural HIV research collaborations using these administrative research documents[93] and made recommendations for selecting approaches that may help forge healthy international HIV research collaborations. Finally, the CAB members will review different drafts of the protocol and provide feedback for further improvement.

Although this current R34 study will be implemented at the Sanpatong Hospital, **we will actively involve stakeholders in the local area.** We have successfully collaborated with the researchers affiliated with the Sanpatong hospital and other service organizations in the local network of HIV care and have developed local CABs and SABs consisting of local Thai PLWH community members, service providers and experts from the areas. From the beginning of the R01 project, we will host CAB and SAB meetings on a regular basis. During the meetings, Drs. Moolphate, Chen, Detels, and Shiu will report study progress, submit documents for review, and discuss topics that need input from the CAB and SAB. The CAB and SAB will share responsibilities in overseeing the project, helping interpret qualitative data arising from the study activities, reviewing intervention adaptation, and finalizing study protocols. We will compare the perspectives from the CAB and SAB and integrate them into the final protocols. The final intervention and operation protocols will be approved by the CAB and SAB, which represent all partner agencies.