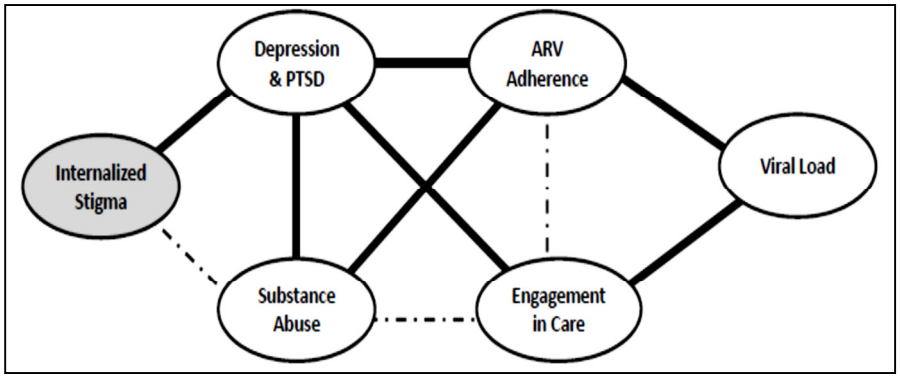
Research Strategy

1. Significance

1a. Stigma is linked with increased HIV morbidity and mortality. Stigma originates from societal and interpersonal processes related to power structures and shared beliefs about the body, health, and illness.[37] Researchers from across scientific disciplines have put forward a set of terms that are helpful in distinguishing types of stigma. *Public* stigma refers to the negative attitudes held by members of the public about people with devalued characteristics. *Internalized* stigma occurs when people with devalued conditions come to believe that negative public attitudes apply to them[38,39] and suffer negative consequences as a result.[39,40] Figure 1 depicts several direct negative consequences of internalized HIV-related stigma: depressive symptoms, post-traumatic stress disorder (PTSD), and substance abuse.[28,41-46,50] In terms of stigma's link to antiretroviral (ARV) medication adherence, Dr. Rao and colleagues found depressive symptoms to be a mediator between internalized stigma and medication adherence.[9] Other research confirms that HIV-related stigma, along with psychological issues including depressive and anxiety symptoms and substance use, are prominent barriers to medication adherence for people living with HIV (PLWH).[7-9,12,14-15,19,21-22,47-49] A major mechanism behind the connection between stigma and poor medication adherence appears to be unintentional disclosure: PLWH find that closely adhering to antiretroviral regimens can unintentionally disclose their HIV status.[7,16] Although studies in the United States have focused more on medication adherence than engagement to care, a handful of studies have begun to connect stigma with poor engagement to care for people with HIV.[22,49,51-54] Furthermore, poor engagement with care and poor medication adherence have both been strongly linked to increased viral load.[23,55-57] Relationships that have been empirically validated are depicted with bold connecting lines in Figure 1 (causal relationships are not assumed). This body of research clearly demonstrates that HIV stigma is linked to poor health outcomes. However, no research exists on the effectiveness of stigma reduction interventions and the impact of stigma *reduction* on depressive symptoms, substance use, medication adherence, engagement to care, and viral load.

Figure 1: Internalized HIV Stigma, Associated Factors, and Poor Outcomes



1b. Stigma is related to disparities in HIV outcomes for African Americans. In 2004, the US Centers for Disease Control and Prevention (CDC) revealed that for nearly a decade, AIDS had been the leading cause of death for African American women between the ages of 25 and 34.[10,11] These staggering mortality rates can be associated with disparities in HIV outcomes, because HIV medication adherence and sustained engagement to care are necessary to achieve positive health outcomes for people with HIV.[14,55-56,58] Indeed, several studies have shown that African American race/ethnicity has been associated with poor medication adherence and engagement in care.[16-17,19,22,54,59] In addition, African Americans living with HIV or AIDS often face multiple stigmas, including stigmas associated with the disease, socio-economic status, and race/ethnicity. This can compound the negative effect of stigma on medication adherence, and ultimately, health outcomes.[60-61] Taken together, the research reviewed thus far suggests that unchallenged stigma may be negatively impacting morbidity and mortality for African Americans living with HIV. Furthermore, **these findings suggest that if we intervene to reduce internalized stigma, we may improve health outcomes for this population.** In fact, many studies, workshop reports, and international health organizations have explicitly recommended that researchers and public health practitioners work to implement effective HIV stigma reduction programs.[21,29,62-64]

1c. Internalized stigma reduction programs have not been examined for effectiveness in large scale trials. Unfortunately, internalized HIV stigma has been the target of very few stigma reduction programs; even fewer have undergone effectiveness evaluation. A recent review of the literature on HIV stigma reduction interventions found only 1 intervention trial focused on reducing stigma among PLWH.[33] Furthermore, the review found no studies that were aimed at reducing *internalized* stigma among PLWH. Our own online web-based and PubMed searches for internalized stigma reduction programs identified only 3 formal programs (those with manuals or materials) in which people living with HIV were or could be the target audience for

stigma reduction. We found that only 1 of the 3 programs had published an evaluation. That program, the Emotional Writing Disclosure intervention, was examined through pilot study.[65-66] The program required participants to write about thoughts and feelings of stressful events experienced. The act of writing the experience down was believed to help participants put their experiences in a more positive light. Abel and colleagues showed that after participating in the intervention, participants' psychological distress decreased. However, a successful intervention for PLWH must be literacy-sensitive.[67] This particular intervention would not be feasible for use with people with limited literacy, as it requires participants to have proficiency with written expression. The second stigma reduction program we found—with no published evaluation—was developed by the National Minority AIDS Council,[68] funded by the U.S. Health Resources and Services Administration. It proposes to work with communities of color to reduce stigma through "action planning." This program relies primarily on a series of slide presentations, and uses information dissemination as its primary mechanism for change. The third program, the HIV Stigma Toolkit, was developed by the International Center for Research on Women (ICRW), the Academy for Educational Development, and the International AIDS Alliance.[34] The Toolkit has been used to reduce public stigma in many countries around the world. It has also been used within the United States (personal communication, Laura Nyblade, formerly at ICRW), but there have been no published evaluations. Of particular note is that the Toolkit has been adapted and used by HPTN 043 Project Accept for stigma reduction in post-test support services within a larger HIV testing and prevention initiative.[35] The Toolkit actually contains modules with exercises developed to provide people with HIV ways in which to cope with internalized HIV stigma. The intervention was developed with stakeholder participation, using participatory action research methods.[34] As we will now describe, it is this intervention that provided the basis for the Unity Workshop.

1d. The ICRW program and the Unity Workshop adaptation contain essential components for stigma reduction. Of the three programs reviewed above, the ICRW program had several components deemed necessary for stigma reduction interventions. Brown, Macintyre, and Trujillo conducted a review of public stigma reduction programs and outlined necessary components. These include: (a) *education*, (b) *contact* with affected persons, (c) *counseling* approaches, and (d) training in *coping skills*.[69] The education component is necessary to counter misinformation that exists about people with HIV and to define stigma; contact with affected persons is necessary to humanize the illness and achieves the fundamental aspect of Corrigan's theory of 'Strategic Stigma Change'[36] counseling approaches provide a modality for implementation; and coping skills training is necessary to help teach people ways to navigate stigmatizing situations.[69] The ICRW intervention contains all of these components, and uses a group counseling format to encourage (e) *social support*, which Simoni and colleagues have identified as an important mechanism involved in reducing depressive symptoms and promoting medication adherence.[70-72] We chose to adapt the ICRW intervention, described below, and through this process we added other components to our intervention, including (f) *active learning* and (g) *modeling* methods. Social Learning Theory tells us that people learn through observation, imitation, and modeling.[73] Thus, in our adapted intervention, workshop participants' ability to navigate stigmatizing situations is promoted through viewing trigger video and peer discussion segments. Furthermore, we adapted the ICRW intervention to leverage contact among PLWH by having peer advocates facilitate the workshop and by increasing peer-to-peer participation.

1e. Our study team systematically adapted the ICRW program for African American women living with HIV. The ICRW program was developed in sub-Saharan Africa, and thus, we needed to tailor the intervention for the African *American* context. Recent research findings have supported our decision to adapt this particular intervention, as culturally tailored interventions have been found to be very effective.[74,75] We conducted focus groups with African Americans living with HIV in Chicago and Seattle to obtain information on their experiences with stigma and which aspects of stigma they would like to see addressed in an intervention. We also analyzed their feedback on the ICRW program's (individual exercises) potential to reduce stigma for African Americans living with HIV. Results from the focus groups have been presented and published[1,76] and details are provided in section 3a6 (Previous Studies) of this proposal. To summarize, women participants described issues of stigma in family, dating, and health care settings that they felt should be addressed in a group format, and male participants suggested that stigma be addressed through an Internet-based format. The women's advice and concerns mapped well onto content included within the ICRW HIV Stigma Toolkit, and thus, we chose to begin our work by developing an intervention with African American women living with HIV. We selected content and adapted exercises based on feedback from these focus groups with women, data that included qualitative responses and rank-ordered preferences for exercises from the ICRW program. Working with this feedback, we then developed 4 "trigger videos" to embed within exercises of the intervention. Dr. Rao and the

research team developed scripts for videos based on scenarios outlined in the ICRW program, reworking and fusing scripts with themes and details provided by women in the focus groups. In this way we were able to make these new video scenarios both locally appropriate and credible.[36]

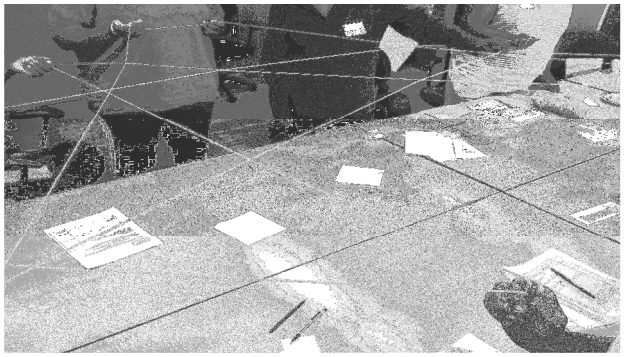
By observing an International Training and Education Center for Health (I-TECH) intervention developed for stigma reduction among health care workers in the Caribbean, we also noted that videos tend to stimulate discussion and engage participants in active learning.[77] With Tom Furtwangler (I-TECH Health Communications Director) and documentary filmmaker James Longley (a MacArthur Foundation "Genius" Fellow) we filmed the 4 scenarios that became our trigger videos (Table 1 provides web links to view these videos).

Table 1. Trigger Video Web Links

"Sisters"	http://www.youtube.com/watch?v=VmghpcEb9kc&feature=related
"Counseling"	http://www.youtube.com/watch?v=xIwmiq7ppaI&feature=related
"Lunchroom"	http://www.youtube.com/watch?v=tCfLExQOWyw&feature=related
"First Date"	http://www.youtube.com/watch?v=vWvXH5tUUhQ&feature=related

1f. The Unity Workshop was successfully piloted. For pilot feasibility study, we ran the intervention in Seattle, Washington, as two sets of workshops for women, lasting about 8 hours total across 2 afternoons (4 hours per afternoon). Each afternoon, our participants engaged in active discussion and stigma reduction exercises. An African American woman living with HIV who worked as a peer advocate in a community- based organization for women living with HIV served as the primary workshop facilitator. She had extensive experience leading support groups and providing testimonials about living with HIV. A master's-level social worker assisted with facilitation and helped to lead break-out group sessions (approximately 8 participants in each smaller group). Dr. Rao, a licensed clinical psychologist, was also on hand in case the women experienced any extreme psychological distress. We began the workshops by discussing group expectations and establishing ground rules. We then asked the participants to discuss what stigma meant to them. The main portion of the workshop focused on discussions and exercises to help participants acquire new coping skills. These exercises covered (a) *practicing relaxation and self-care*, (b) *sharing coping strategies* from other group members, (c) *viewing trigger videos* and (d) *discussing how to handle potentially stigmatizing situations* with family, in the workplace, and in other settings, and (e) *role playing ways to navigate these difficult situations*. We also developed an intervention manual with detailed instructions on how to move through the exercises in the workshop; a copy is provided in Appendix 1. Several of the exercises were conducted in smaller break-out sessions. We did this to facilitate in-depth discussions of topics and encourage participation and discussion from quieter members of the group. In the last exercise of the first afternoon session, the women formed a "web of string," in which one group member tossed a ball of yarn to another group member after calling out a positive quality about herself. We then asked the women to generate names for the web that had been created and linked them together. The women called out, "peace," "togetherness," and finally, "unity." Thus, we named the workshop the "Unity Workshop," after the web that symbolized the empowerment that comes about through social support. A picture of the web is provided in Figure 2.

Figure 2: Web of String Exercise



2. Innovation

The proposed study will be the first randomized controlled trial of an internalized stigma reduction intervention. Various groups have used the ICRW HIV Stigma Toolkit, which formed the basis for the Unity Workshop, but none have systematically evaluated or published findings on the efficacy of the program. In addition, we believe that our adaptations (tailoring it to experiences of African American women living with HIV, using videos based on real life scenarios to trigger discussion, and having a peer advocate moderate the workshop) represent important enhancements to the Toolkit program. Our pilot study participants reported that workshop exercises and themes discussed were directly relevant to their struggles. Our hypothesis is that our workshop's culturally tailored, multimedia intervention, coupled with its peer-led discussions, support, and skills practice, will help to reduce internalized stigma for African American women living with HIV. In doing so, it has the potential to make a positive impact on HIV morbidity through improved medication adherence and sustained engagement in care. **We will explore previously unexplored mediators and moderators between stigma reduction and health outcomes**. Although psychological factors (e.g., depressive

symptoms, PTSD, and substance use) have been tied to stigma and medication adherence,[9,16,28,59,78] little is known about the association between stigma *reduction* and these psychological factors. We will also examine the impact of stigma reduction on engagement in care, medication adherence, physical health biomarkers, and other previously unexplored factors.

3. Approach

3a. Preliminary Studies. **Dr. Rao is an early career investigator and the proposed study is the follow-up to her career development award**. She conducted her postdoctoral research fellowship at Northwestern University (NU), Chicago, and had a primary faculty appointment there until moving to the University of Washington (UW), in Seattle. Dr. Rao maintains an adjunct faculty appointment at NU. She has conducted several studies with the HIV Clinic at Northwestern University and is familiar with their clientele, recruitment challenges, and institutional review board processes. In addition, Drs. Simoni, Crane, Mugavero, and Cohn have worked in the area of HIV and women, HIV-related stigma, HIV medication adherence, and engagement in HIV services in independent studies or in collaboration with Dr. Rao. Key studies that have led to this proposed study are described below, in chronological order from oldest to most recent studies conducted.

3a1. African Americans experience a culturally specific form of HIV stigma, impacting medication adherence. Dr. Rao and colleagues found that youth living with HIV (24 out of 25 identified as African American) identified stigma as a barrier to medication adherence.[7] Fifty percent of participants indicated that they skipped doses because they feared unintended disclosure of status. In another study, Dr. Rao and colleagues used novel psychometric techniques to find response differences between African American and white PLWH on the Berger HIV Stigma Scale.[79]

3a2. Women from vulnerable populations experience interpersonal violence, which compounds psychological symptoms. Drs. Rao and Turan have explored issues around interpersonal violence among poor women and women living with HIV. Dr. Rao recently found associations between interpersonal violence and depression among poor women in India,[80] and was awarded pilot funds to examine the impact of perinatal domestic violence on birth outcomes in India. Dr. Turan has also focused her work on reducing HIV stigma to improve engagement in care and overall health of women both domestically and internationally.[81-82]

3a3. Peer-led interventions are successful in improving medication adherence among people living with HIV. Dr. Simoni has been involved in developing and evaluating peer interventions throughout her career. In her recent work, she has developed effective peer interventions to promote HIV medication adherence among PLWH in New York City and Seattle.[70-72,83-89] The peer program was selected by CDC as one of the few HIV medication adherence programs to meet standards of "good evidence," and will be available for online dissemination.

3a4. Dr. Rao and team developed a measure of internalized stigma validated with African Americans living with HIV. Dr. Rao and team developed the Stigma Scale for Chronic Illness (SSCI), a "generic" scale developed to assess stigma internalized by people with a variety of conditions. We developed a 24- and an 8-item version with good psychometric properties that were validated using item response theory techniques for use with people across neurological disorders (e.g., epilepsy, stroke, multiple sclerosis).[90-91] We conducted cognitive interviews to elicit feedback on the SSCI's relevance and applicability for African Americans living with HIV.[92] Results led us to remove certain items to improve the relevance of the scale,[93] resulting in a 14-item scale. The 14-item SSCI demonstrated good psychometric properties (Cronbach's alpha was 0.93, Pearson correlation with HIV Stigma Scale[94] was 0.76) in measuring internalized and enacted stigma among African Americans living with HIV.[2]

3a5. Dr. Rao and team related HIV stigma, depressive symptoms, and medication adherence in a structural equation model. In another rigorous study, Drs. Rao, Simoni, Crane, and others linked HIV stigma, depression, and medication adherence in a structural equation model (N=720 participants).[9] In independent models, we found that poorer adherence was associated with higher levels of stigma and depressive symptoms. In the simultaneous model that included both stigma and depressive symptoms, depression had a direct effect on adherence, but the effect of stigma on adherence was non-significant, suggesting that depressive symptoms fully mediated the association between HIV-related stigma and HIV medication adherence. In addition to this work linking stigma, depressive symptoms, and adherence, Dr. Crane is involved with a line of work assessing the role of depressive symptoms among people with HIV.[95-98]

3a6. Focus group feedback guided the adaptation of stigma reduction strategies among African Americans living with HIV.[3] We conducted focus groups with African American men and women living with HIV in Chicago

and Seattle to obtain information on their experiences with stigma, and to discover which topics they would like to see addressed in an intervention. We also asked for their opinions on the ICRW exercises' potential to reduce stigma. In broad summary, women described pressing issues of stigma reduction around family and dating that should be addressed in a group format, and men suggested that stigma be addressed through an Internet-based format. We focused our analysis on the results from women, in order to guide the adaptation of the ICRW intervention. We did not find systematic differences in responses from women in Chicago or Seattle. Themes that evolved from the discussions with women were (a) the importance of family and community support (or lack thereof), (b) the moral judgments of health care workers, friends, and family members, (c) trust within social networks, (d) misconceptions among members of black communities, and (e) multiple stigmas and racism, particularly within treatment settings. Women agreed that support groups, particularly discussions with other women who had managed similar experiences, had the potential to reduce internalized stigma. The women also filled out forms in which they rank ordered ICRW intervention exercises by preference, and this information guided inclusion of exercises into the adapted intervention.

3a7. Engagement in care impacts HIV-related morbidity. Dr. Mugavero has conducted research studies evaluating the roles of stigma, disclosure, and coping, and their impact on health outcomes among people living with HIV in the southern United States (primarily African Americans).[64,78,99] In one recent study, Dr. Mugavero and colleagues found appointment non-adherence to be a mechanism by which African American racial-ethnic background is associated with virologic failure.[54-55,100]

3a8. A pilot feasibility study of the Unity Workshop shows promise in reducing internalized stigma. Overall, we were able to recruit 24 women; 21 women (88%) returned for the second session of the workshop and 19 women (79%) completed the 1-week follow-up assessment. There were no negative comments made when feedback on the workshop was elicited, and responses detailed the level of emotion in the room during the workshop and how personal differences gave way to a sense of unity and support. The women indicated that they felt empowered by the social support and lessons learned from others going through a similar experience. One woman commented, "I liked it a lot. I got to know more people and learned a lot about myself and stigma. The first day was emotional but the second I was much more open. Most of the situations I have personally dealt with. It made me open up and release issues I have been holding for the last 10 years, and talking with others, I don't feel so segregated." Another participant commented, "I enjoyed the stigma group very much. I was a little late but I had bus transportation problems. The location was great. I can be naturally shy, but when asked, I can usually speak out. Sometimes I don't relate to the women as much as I would like because I am very young and have a very unique background. It helped to speak out about status to other women more than anything." In addition to this positive feedback, we observed that when videos ended, all the women spoke at once to express their reaction to the scenarios, demonstrating active learning. We also noticed women exchanging phone numbers to reconnect outside of the study, strengthening their social support networks. To assess quantitative outcomes, participants were asked to complete the 14-item Stigma Scale for Chronic Illness (SSCI), which suggested that the Unity Workshop reduced internalized stigma among African American women living with HIV. Overall, the 24 women's total stigma scores decreased from baseline (Day 1: $M = 38.0$, $SD = 11.4$) to Day 2 ($M = 32.7$, $SD = 13.7$), and from baseline to Day 8 ($M = 34.2$, $SD = 11.7$). Paired t-tests indicated statistical trends were present for changes in stigma scores from baseline to Day 2 [$t(20) = 2.05$, $p = 0.05$], 95% confidence interval [CI]: -0.10 to 10.76) and baseline to Day 8 [$t(18) = 1.95$, $p = 0.07$, CI: -0.36 to 9.83).[71] **These results were orally presented at the XIX International AIDS Conference in Washington DC and are described in a manuscript recently accepted for peer reviewed journal publication.**[1,76]

3b. Peer Advocate Selection and Training. In the proposed study, we will be implementing the Unity Workshop in Chicago and Birmingham. As such, we will first select peer advocates and then train peer advocates in basic counseling techniques. We will also train a clinic-based social worker and the peer advocate in Unity Workshop implementation. Our peer advocate in Seattle (T. Rasberry) who led the pilot Unity Workshop, works with a community-based organization (Babes Network YWCA). At this organization, she has had extensive experience leading support groups and providing testimonials about her experiences living with HIV. In this proposal, we will leverage Ms. Rasberry's considerable skills as a peer advocate, and she will lead peer advocate training for this project. We will identify 2 African American women living with HIV through health care providers in the clinic, one in Chicago and one in Birmingham, to serve as peer advocates. They will be recruited based on their connection to support networks for PLWH, public speaking skills, good medication adherence and engagement in care, and their interest in serving in this role. The social worker and peer advocate will be given workshop materials to study before training begins, and we anticipate the trainings will take 2 days at each site. Ms. Rasberry will lead onsite training for the peer advocates in basic counseling

techniques and in the facilitation of the Unity Workshop. We will use a shortened version of the peer "buddy" training manual (provided in Appendix 2) from Dr. Simoni's NIH-funded medication adherence intervention study to train peer advocates (R01 MH058986). Dr Simoni's peer "buddy" training program will be shortened to cover one day of training, to include awareness of confidentiality, basic counseling skills, and knowing when to refer to a health professional. This training will not cover adherence counseling techniques. The site social worker will participate in the Unity Workshop facilitation training (Day 2) alongside the site peer advocates. Ms. Rasberry will again lead this training. The Unity Workshop manual is also provided in Appendix 1. **During both trainings, Dr. Rao will observe Ms. Rasberry's fidelity to the peer and workshop training manuals**.

3c. Communication and Meeting Schedule. The UW, University of Alabama Birmingham (UAB) and NU sites are AIDS Clinical Trials Units with fully-functioning community advisory boards (CABs). **Dr. Rao and site principal investigators will attend CAB meetings on a quarterly basis**, in person or by phone to describe study processes, seek ongoing feedback, and disseminate results. Furthermore, study investigators will have a monthly conference call to discuss recruitment and study process, and research coordinators will have a twice-monthly conference call with Dr. Rao and a Seattle-based research assistant to discuss study recruitment and process. The Seattle-based research coordinator and peer advocate will have a regular post-intervention call with peer advocates to go over fidelity to study materials and promote inter-facilitator reliability of group moderation methods. We will use Adobe Connect software during these meetings to facilitate visual communication of data and information. UW has a site license to use Adobe Connect and remote users can log in to the UW system free of charge. In addition to these phone meetings, Dr. Rao will travel to the Chicago and Birmingham sites twice per year to monitor study progress and provide technical assistance.

3d. Study Design and Methods

3d1. Overview of design. We will be conducting a randomized controlled trial using a repeated measures design. We will recruit women in blocks of 28. Once we have identified 28 women who would like to participate, they will participate in a baseline visits. We do not anticipate cohort effects within the site (i.e. differential response to intervention by recruitment wave), but we will test for them in our analyses. During a baseline visit, participants will provide informed consent, complete baseline measures, and then receive their (randomized) assignment to a group (Unity workshop or attention control). Participants will complete assessments in individual meetings and attend intervention sessions in groups of 14 participants. After baseline assessment, they will then participate in their assigned group and follow-up assessments as outlined in Table 3. We will then begin recruitment for another 28 women, anticipating that we will begin a new cohort of women in the study every 4 months. Follow-up visits will be made every 4 months, +/- 2 weeks, in order to align with standard of care for frequency of physician visits. All participants, whether in the Unity workshop group or attention control, will complete study measures every 4 months over a 1-year time period.

Table 3. Design for Proposed Study at Each Location*

	Cohort 1 (n = 28)	Cohort 2 (n = 28)	Cohort 3 (n = 28)	Cohort 4 (n = 28)
Month 0	A, GG, A	--	--	--
Month 2	--	--	--	--
Month 4	A	A, GG, A	--	--
Month 6	B	--	--	--
Month 8	A	A	A, GG, A	--
Month 10	--	B	--	--
Month 12	A	A	A	A, GG, A
Month 14	--	--	B	--
Month 16	--	A	A	A
Month 18	--	--	--	B
Month 20	--	--	A	A
Month 22	--	--	--	--
Month 24	--	--	--	A

**Note:* [GG] indicates timing of the Unity Workshop or Attention Control Group (held concurrently). [B] indicates timing of 1-session booster implementation, [A] indicates baseline or post-intervention assessment, [--] indicates no assessment

3d2. Attention control group. Half of the participants will be randomly allocated to participate in attention control groups. The attention control participants' data will serve as a comparison for the Unity workshop participants' data. The attention control participants will take part in a program called "Taking Care of Ourselves and Each Other,"[101] a program about breast cancer screening developed for African American women that uses a similar format and time frame as the Unity workshop. The attention control participants will view a video and discuss in groups their attitudes around undergoing mammogram procedures. The control groups held during the same week as the Unity workshops and control group participants will complete assessments on the same schedule as the Unity workshop participants (See Table 3). We chose a control group on the topic of breast cancer screening because the program used a similar structure as the Unity workshop (e.g. videos, discussion). In addition, although breast cancer may be associated with stigma, we

anticipated that breast cancer stigmas would not be related to *HIV-associated* stigma, which is our primary outcome of interest. A research coordinator will moderate the attention control groups comprised of 14 African American women living with HIV. Like the Unity workshop, the attention control groups will be held near the HIV Clinic setting, such that the full resources of the medical center are available.

3d3. Design considerations. The initial trial will occur in Chicago, and once recruitment and workshop implementation have been completed there, we will begin the trial in Birmingham. We will be staggering the rollout of the workshops and assessments at the 2 locations in order to control workflow for Seattle investigators and consultants. We considered it more feasible to provide technical assistance and training in Chicago first and then Birmingham, rather than attempting to do this simultaneously at both sites. We will use individual randomization within each site (Chicago and Birmingham), in order to minimize confounds within clusters that are apparent with cluster (or group) randomized designs. Six months after Unity Workshop implementation, the women will participate in a booster session. We noted a slight increase in levels of stigma in our pilot study in follow-up assessment after workshop participation, and thus, we decided to include a booster session to help participants solidify stigma reduction techniques. Six months after workshop participation, the social worker and peer advocate will hold a 2-hour booster session. The facilitators will begin by checking in with participants, establishing group expectations, inquiring about their experiences over the past 6 months, and having participants guide them on which exercises and discussions they would like to engage in again. Participants in the attention control groups will not participate in a booster session. Table 3 shows the schedule of assessments and workshop rollout.

3d4. Location. For the proposed study, we selected urban locations where African Americans make up large segments of the population, in order to find large numbers of eligible women who reside within easy access to study sites. Northwestern University in Chicago and University of Alabama Birmingham were chosen in part because of the University of Washington's longstanding collaborations with investigators at the two sites. Dr. Deepa Rao completed her postdoctoral work at Northwestern in Chicago, retains a faculty appointment there, and knows the HIV Clinic at Northwestern well. The Northwestern HIV clinic was also a site in which we conducted preliminary work to adapt the intervention and assessment tools. We will be conducting assessments and holding workshops/groups in rooms within and nearby the HIV clinics. This setting was chosen in order to be convenient for participants who might also be attending medical appointments. In addition, nearby clinic settings have physicians close at hand in case of emergency and resources such as group meeting spaces. During formative phases of this line of research, we asked African American women living with HIV in Seattle where they preferred to have workshop meetings held as part of the focus group discussion. The participants overwhelmingly preferred to have study visits near the HIV clinics where they visited their physicians and case managers on a regular basis. They felt this would be more convenient to them than sites out in the community. We anticipate few confounds in comparing data from African American women living in Chicago and Birmingham, although we will examine location interactions in our analyses. Both Chicago and Birmingham are the largest cities within their states that are surrounded by suburban and then rural areas. The 'Great Migration' between 1910 and 1970 saw many African Americans resettle from the Southeastern to the Midwestern United States, and thus there are likely cultural similarities.[102] More specifically, the HIV clinics at both Northwestern and the University of Birmingham are both University based clinics that see people living with HIV with both private and public health insurance. The NU clinic primarily serves people who reside in urban, Cook County 1,600 square miles. The UAB clinic primarily serves people from urban, Jefferson County, covering 1,100 square miles. Preliminary work on the Unity workshop was conducted in urban-based clinic settings. Thus, we considered it important to conduct the clinical trial in a similar setting, as people with HIV from rural settings likely have different issues to face around stigma

Table 4. Basic socio-demographic characteristics of clinic patients

		Chicago (N= 1625)	Birmingham (N= 1947)
Ethnicity	Caucasian/White	41%	45%
	Black	33%	53%
	Hispanic	8%	1%
	Asian	1%	0.2%
	American Indian/Alaska Native	0%	0%
	Unknown	17%	0.4%
Age Group	14-30	11%	25%
	31-50	56%	63%
	51-70	31%	11%
	71+	2%	0.1%
Insurance	Private	55%	39%
	Medicare	22%	18%
	Medicaid	15%	9%
	Other (Uninsured/Self Pay)	2%	34%

reduction and engagement in care (e.g. structural barriers brought about by distant locations of clinics and lack of public transit). Other aspects of the clinic population are also very similar (e.g. men comprise 78% of the populations at both clinics). Table 4 shows other similar basic socio-demographic characteristics for both the Northwestern University and University of Alabama Birmingham clinics.

3d5. Recruitment. In both Chicago and Birmingham, in order to ensure enough time to recruit 112 participants per site, **we will begin recruiting 4 months before data collection is to begin**. Institutional review board-approved signs will be hung at all clinics advertising the study, and physicians will convey information on the study to eligible potential participants. Signs, physicians, counselors, and nurses based in the clinic will encourage eligible participants to call research coordinators for information on the study. In addition, a research coordinator will be paged, such that when eligible women are appear for appointments s/he will come to the clinic and verbally describe study procedures for eligible and interested participants. Research coordinators will ask potential participants about preferred workshop time of day (morning, afternoon, evening) upon initial phone contact, and investigators will chose a time of day based on responses from potential participants and study staffing constraints. We will begin the first intervention and control group when we have 28 women who have agreed to participate. We will begin the next set of groups after another 28 women have agreed to participate. We anticipate that a new set of groups will begin approximately every 4 months.

3d6. Feasibility of recruitment and detail on sites. Data from our pilot study (implemented with 24 women participants in Seattle) provides useful context for the recruitment rates outlined for the proposed study. Over the course of two weeks, we recruited from the UW publicly funded HIV-clinic, which sees approximately 2,000 patients total in a one year period. Approximately 200 of these patients were African American women living in rural and urban areas of the Puget Sound region (spread across 4,000 square miles of Pierce and King Counties). Approximately 40% of those eligible called the research coordinator with interest in the study. Of those who contacted the research coordinator, 50% participated in the intervention. We did not follow up with women who did not appear for the baseline assessment. To further improve on our rates of participation, we have scheduled at least three months to recruit women at each site, and will follow up with women who do not appear for study visits. **Overall, we expect that the Chicago and Birmingham locations combined will have about 700 African American women as potential participants.**

In Chicago, NU's HIV clinic sees about 1,600 patients in a 1 year time frame; about 225 of these are African American women. In past work, Dr. Rao has quickly and easily recruited 40 women for focus groups and individual interviews from the NU clinic. These women will again be eligible for the present study, and we will take time to recruit others. In addition, Northwestern has formed a close clinical and research collaboration with the Christian Community Health Centers, which is a publicly funded primary care facility with a HIV clinic hours staffed by Northwestern HIV clinic physicians. The Christian Community Health Center HIV clinic sees about 200 people living with HIV, all African American, with about 1/3 being women. This would increase our potential participant pool in Chicago to 300. We would like to conduct half of our workshop and attention control groups at the NU clinic and half at the Christian Community Health Center clinic site, while alternating which of 2 peer advocate moderators lead Unity workshops at each site and examining site and moderator effects in our analyses. In Birmingham, the UAB clinic sees approximately 2,000 patients in a 1 year time frame; 400 are African American women. Drs. Crane and Mugavero have already begun routine patient reported outcomes data collection as part of R01MH084759 (PI: Crane), and have collected over 11,000 clinical assessments to date.

3d7. Study participants. Women will be eligible for inclusion in the study if (a) they identify as having an African American racial/ethnic background, (b) they are at least 18 years of age or older, and (c) documented HIV positive status. We will include women who are African born, of Afro-Caribbean descent, or identify as Black Latino, as long as they have been living in the United States for at least 10 years. We considered including women who had migrated more recently to the United States, but decided it was best to exclude more recent immigrants in anticipation of culturally specific issues tied to their countries of origin around HIV stigma that need unique attention in stigma reduction interventions. In addition, we anticipate that some participants will not yet be prescribed antiretroviral medications. We will include these women in order to gather data from people with a range of experiences living with HIV in the study. We will be missing medication adherence data from participants not yet on antiretrovirals, but given the percentage of people on treatment in both clinics (80-90%), we expect to have a large enough sample of people on antiretroviral medications to perform analyses for aim 2. This point is described further in the section below addressing sample size issues for aim 2.

3d8. Participant measures (all aims). The study measures are listed in Table 5 (with numbers of items for each measure), and draft versions of these measures are provided in Appendix 3. The research assistant will schedule study visits at 4-month intervals, +/-2 weeks, for flexibility in retaining participants who have busy schedules. Assessments will be completed during workshop and assessment-only visits. All measures will be administered through the Audio Computer Assisted Self Interview system (ACASI), through which participants hear questions and response choices through headphones. This method has been proven feasible and beneficial in our work and in situations where participants have limited literacy.[2,103-104]

All participants will provide socio-demographic and clinical information (i.e. age, time since diagnosis, transmission risk factor) at their baseline visit in the study. All other measures will be administered at baseline, immediately after intervention participation, and 4 months post intervention for 1 year. The research coordinator will obtain information on CD4+T cell count, and viral load from the participants' medical records at each study visit. Internalized stigma will be measured using the Stigma Scale for Chronic Illness[90] to assess internalized and experienced stigma. Cognitive interviews and psychometric data support the use of this scale among African Americans living with HIV.[90,93] Medication Adherence will be reported in two ways. First, *physician report* of poor medication adherence will be obtained from the medical record every 4 months. Second, participants will *self-report* medication adherence on the following items every 4 months. Three items are modified from the Adult AIDS Clinical Trial Group medication assessment,[18,105] including the number of doses missed in the previous 4 days (response options range from "0" to "more than 4"), missed doses on the previous weekend ("yes" or "no"), and time of last missed dose (response options range from "within the past week" to "never skip medication"). Patients will be asked to rate their ability to take their HIV medications over the previous 30 days (response options range from "very poor" to "excellent"). Finally, patients will be asked to rate their HIV medication adherence over the past 30 days on a visual analog scale (0% to 100% range).[102,103] Our team members have used these items extensively in our work,[9,106] which were found to have less bias than other medication adherence items.[107-109] To assess engagement to care, all HIV-related visits (e.g., medical, counseling) attended in the last 12 months will be extracted from the medical record at baseline. HIV-related visit attendance over a 4-month period will be extracted from the medical record at each study visit for information on engagement to care. In each case, visits attended divided by the total number of appointments scheduled will be considered the measure of engagement in care. We will take into account only missed visits, not rescheduled visits. Depressive symptoms and a provisional diagnosis of Major Depressive Disorder will be assessed with the Patient Health Questionnaire (PHQ-9).[110] Given the high prevalence of depression and substance use among people with HIV,[114] we will administer both scale to all participants at all assessment visits. The scale is brief and is validated for use among people with HIV. Our team has used it extensively in our work.[7,91,96] To measure substance use, we will use the Substance Abuse Mental Illness Symptoms Screener (SAMISS),[111] which was developed to assess substance abuse among PLWH and the Alcohol Use Disorders Identification Test (AUDIT)[112] to measure alcohol consumption, drinking behavior, and alcohol-related adverse reactions and problems at each assessment visit. AUDIT has been used with PLWH.[113] In addition, considering that many of the women may have trauma histories,[95] we will assess for post-traumatic stress disorder (PTSD) using the PTSD checklist at baseline.[115] If a participants scores 50 or higher on the PTSD checklist, indicating a probable diagnosis of PTSD, then the checklist will be given to measure symptom severity post-intervention and at each follow-up assessment. Finally, we will measure perceived social support, as we have theorized it to be one of the mechanisms by which the Unity Workshop promotes stigma reduction. We will use the 19-item Medical Outcomes Study-Social Support Survey (MOS-SSS), a multidimensional measure that has been used internationally to assess perceived social support in chronic disease contexts.[116]

Table 5. Study Measures

	Modality
Socio-demographics	8 items
CD4 +T cell count	Medical record
Viral load	Medical record
Engagement in care	Medical record
Internalized stigma	14 items
Medication Adherence	5 items + physician report
Depressive symptoms	9 items
Substance use	17 items
PTSD checklist	17 items
Social Support	19 items

3d9. Procedures (all aims). Workshops and assessments will take place in rooms (e.g., classrooms, clinic interview rooms) within the medial centers and near the HIV clinics at both sites (Chicago and Birmingham). Research coordinators will obtain informed consent before participation, including consent to participate in the 2-afternoon workshop, complete self-report measures every 4 months for 1 years, have workshops audio recorded, and have information extracted from their medical record on visit attendance. Once participants are enrolled, the research coordinators will attempt to schedule individual study visits (for assessments only) such

that they are aligned with the women's regular clinic visits with their physician. Workshops will be scheduled over 2 consecutive days at times announced to participants at randomization. Once 28 participants have agreed to participate, participants will be randomly assigned to one of 2 groups, the Unity workshop or Attention Control group. A computer program will generate participant assignments based on random numbers in blocks of 2. Participant assignments will be sealed in an envelope with study identification number and opened after participants have completed baseline measures. The research coordinator will administer measures at each study visit (every 4 months), regardless of whether the participant was in the intervention or control group. The measures will be programmed into an Audio Computer Assisted Self Interview (ACASI) format, and participants will complete measures by hearing questions through headphones and responding onto a computer touchscreen. The research assistant will be sitting in the same room with the participant to assist with issues that may come up with assessments (e.g. understanding computerized format, trouble-shooting computer problems). The research coordinator will also obtain information specified from the medical record immediately after each visit. The workshop will be implemented across 2 consecutive days, as in the pilot study and as outlined in the workshop manual (Appendix 1). In addition, 6 months after workshop participation, the social worker and peer advocate will hold a 2-hour booster session. Participants will receive $20 after completing measures during assessment-only visits and $50 for each workshop or booster session. The women will be paid more for workshop and booster sessions than for assessment-only in order to attend sessions that will be 2-4 hours (significantly longer than assessment sessions) in duration. Study coordinators will keep track of payments and attendance for each visit.

3d10. Data Analyses and Sample Size Calculation for Aim 1. Baseline demographic characteristics and measures across randomization arms will be compared to determine adequacy of randomization or potential confounding. Intent-to-treat analyses will be used to compare outcomes. Our primary outcome of interest is change in total internalized stigma scores **[Aim 1: Determine the long-term effectiveness of the Unity Workshop to reduce internalized stigma for African American women living with HIV]**. We will first conduct preliminary analyses to test whether the interaction between treatment effects and cohorts/sites is statistically significant. If they are not significant, these interaction terms will be excluded from further analyses. Stigma reduction will be analyzed using linear mixed models (LMMs). LMMs allow for analysis of within and between group variance and are recommended for analyzing clustered data obtained from trials.[117] In the LMM models, stigma will be regressed on treatment group (Unity workshop or control), time, and the treatment by time interaction. In order to determine needed sample size, we turned back to our pilot feasibility study, in which Cohen's d was calculated at 0.42. Cohen states that power in large scale trials should be sufficient to detect the small-to-medium effect sizes (defined as standardized effect sizes between 0.2 and 0.5).[118-120] Given that our pilot feasibility study demonstrated a trend and not statistically significant differences in mean total stigma scores, we chose to calculate sample size with the conservative effect size of 0.2. With power set at 85%, alpha set at 0.05, 3 follow up assessments, repeated measures correlated at r = 0.5, and effect size (for mean differences) set at 0.2, we will need a total sample size of 94 to detect a clinically important difference between participants' scores pre- and post-intervention within one location. We will recruit at least 94 participants at each location in order to fully examine stigma reduction within each location (without pooling the data). **Anticipating 15-20% dropout, we will enroll 224 participants in the study (112 in Chicago and 112 in Birmingham) and still have approximately 83-85% power to detect differences in outcomes.** Table 6 shows sample size calculations, varying the value for power and using the values for effect size and alpha specified above.

Table 6. Sample Size and Power

Power	Sample Size (Total Across Sites)
0.91	224
0.89	210
0.87	198
0.85	188
0.83	179

3d11. Sample Size and Data Analyses for Analyses of Secondary Outcomes (Aims 2 and 3). In examining mediation across variables [**Aim 2: Examine whether stigma reduction is associated with improved physical health (2 variables), mediated by reduced psychological symptoms (3 variables), improved engagement in care and medication adherence**], we will conduct Structural Equation Modeling (SEM) using Figure 1 as a basic model to confirm with data from African American women living with HIV. As a rule of thumb for conducting SEM, data from 200 participants overall or 20 participants per variable of interest are considered a minimum.[121-122] In our case, we are interested in examining 8 variables, and thus analyzing data from all participants in the study would be ideal. The Northwestern University and Christian Community Health Center Clinics have approximately 80% of patients on antiretroviral medications, while the University of Alabama Birmingham clinic have approximately 90% of patients on antiretroviral medications. Thus, we expect to have medication adherence data on about 190 participants, enough participants to conduct secondary

analyses on medication adherence data. In analyses between mediating variables (also Aim 2), we will use generalized estimating equations (GEE) to analyze these non-normally distributed outcomes. In order to examine the impact of the intervention on levels of depressive symptoms, substance use, and PTSD symptoms, we will also use LMMs. GEE is known to work well with longitudinal percent adherence data, and LMMs will allow us to examine both with and between group variance.[117] Furthermore, in analyzing moderator variables **[Aim 3: Explore whether stigma reduction due to the intervention is moderated by location, transmission risk factor, time since diagnosis, and perceived social support]**, we will be extending the primary outcome analysis by including the treatment group (Unity workshop vs. control) by location (Chicago vs. Birmingham) by time interaction, and determine if location as an effect modifier in the LMM analysis. We will examine other potential moderator variables of interest (time since diagnosis, transmission risk factor, social support) in a similar model.

3d12. Missing data (all aims). Missing data may occur in the proposed study in two ways. First, missing data may occur in terms of item responses. In the likely case that item responses are missing, we will prorate total scores on individual measures by taking an average score on the measure and multiplying by the total number of items on the scale to produce a total score for the scale. Second, missing data can occur from loss to follow-up, or dropout, in the study. Prior to performing analyses, we will evaluate the amount, reasons, and patterns of missing data. If the reason for missing data is not related to the endpoint of interest, then the missing data are considered to be missing completely at random (MCAR).[120,123] If the missing data depend on observed outcomes, then the data are considered to be missing at random (MAR). To test for MAR, we will compare the baseline characteristics of patients with and without complete data. We will create an indicator variable to denote whether or not the assessment was completed at each visit, and then use logistic regression models to determine whether the previously obtained measure is associated with the probability of missing data at the next visit. If missing data is considered to be MAR, then we will evaluate the need to use multiple imputation. Likelihood-based mixed linear models and GEE models will give valid results if dropout is MAR. Weighting of cases by the probability of dropout can be used to correct inference for GEE models.[124,125] Sensitivity analyses will be conducted to determine the impact of dropout.[126,127]

3d13. Process Outcome Data Collection (Aims 1). We will examine process outcomes in order to determine extent of fidelity to workshop materials and barriers and facilitators to implementation of the workshop in Chicago and Birmingham.[128] In order to examine these outcomes, we will digitally audio record workshop proceedings during each session to ensure standardization of activities. After each workshop session, the audio recording will be encrypted and transferred electronically to a Seattle research assistant, who will check that the facilitators maintained fidelity to the intervention by checking that all exercises were conducted.[129] Immediately after the last follow-up visit is completed at each site our study coordinators randomly select 10% of Unity Workshop study participants to interview by phone and inquire about implementation challenges. At each site, we will use a random number generator to select participant numbers between 1 and 56 (number of participants randomized to Unity Workshop at each site, regardless of drop out). During the interview, we will ask about satisfaction with the workshop and barriers and facilitators to their attendance, participation, and the workshop's success (Appendix 3). The coordinator will take detailed notes during the phone conversation. In addition to participant interviews, workshop facilitators (N = 4) will keep process notes about their experience as the workshops are implemented, and write brief reports on process of workshops for the site study coordinator (who will subsequently submit reports and brief the principal investigator during regular meetings). After the trial period has ended, they will complete a report describing issues that arose within workshops, barriers and facilitators of workshop activities, and provide their feedback on the program's sustainability within their clinics.

3d14. Qualitative Data Analysis of Process Outcome Data (Aims 1). Our approach will provide a means of data triangulation, eliciting information from more than one source and modality, in order to enhance the validity of the data.[130] We expect that interview data from 44 participants, 2 social worker workshop facilitators, and 2 peer advocates will be enough to reach data saturation (no new information emerges from the interview), given the narrow focus of the interview topic.[131] Dr. Rao, experienced in both qualitative data analysis techniques,[7,93,132] will supervise in the thematic analysis of the coordinator and facilitator notes and reports. The Seattle-based research assistant will independently code the reports and notes, identifying themes and sub-themes in an iterative process over multiple readings of the material.[133] Drs. Rao, Simoni, and the research assistant will meet to discuss themes developed, and clarify any unclear working or structure of themes and sub-themes. We will develop a table summarizing the qualitative data, separating themes by Chicago and Birmingham locations. All investigators will review the table individually and will also meet

collectively to prioritize the suggestions and identify potential modifications to future workshop activities. The themes identified will guide subsequent procedures for implementing future groups.

3e. Data and Safety Monitoring Plan. Upon funding and prior to data collection, we will institute a Data Safety and Monitoring Board (DSMB) to monitor this trial. This DSMB will include at a minimum four professionals outside of the study with expertise in the following domains: treatment research, psychopathology, HIV related pharmacotherapy, health disparities, biostatistics, and ethics. The DSMB will convene for a full meeting twice annually via telephone to review data and safety records and prepare a report for each of the three (UW, NU, UAB) institutional review boards (IRBs). Personnel at all three sites will follow their institutional policies for reporting serious adverse events (SAEs) and adverse events (AEs) to the IRB, the DSMB, and to NIMH. At least two weeks prior to each DSMB meeting, the Seattle based Research Coordinator will prepare a report to be reviewed during that meeting. The report will include the number of participants who signed consent forms for the study and were randomized, the number of post-randomization dropouts, reasons for these dropouts, and any safety concerns, adverse events, etc. An up-to-date consent form will be provided, as well as a summary of measures taken to protect confidentiality (e.g., data and tape storage, use of coded ID numbers, etc.). Interim analyses will be conducted and provided in the report. An interim analysis will be performed at the half way point of data collection in Chicago and Birmingham. The DSMB members will provide feedback on their concerns and comment on any modifications in protocol that may be necessary. More information on the DSMB and its meetings are given in the human subjects section of this proposal.

3f. Limitations. The study results will depend heavily upon the participants' commitment to the project and active participation in the workshop. In order to cultivate this, we have placed much emphasis on appropriately selecting and training facilitators and research staff to keep participants engaged. In our experience before and after pilot study, when we have presented information on the workshop, members of African American communities have been enthusiastic about the project and its widespread implementation. In addition, 2 pilot study participants joined a weekly support group soon after study participation. We will leverage this history and bring a personal touch to study implementation by helping the women feel connected (e.g., through greeting cards, phone reminders) and encouraging strong ties with other participants. Thus, we feel that the project will move forward and is likely to garner enthusiasm and commitment from clinic staff, health care workers, community advisory board members, and participants. We will standardize this process and measure when incentives are given in order to examine its impact on the outcome.

3g. Strengths. The strengths of this study include the fact that it is the first study of its kind aimed at reducing internalized stigma and that it will examine stigma reduction longitudinally in a full scale randomized controlled trial. In addition, we will be studying an intervention that has demonstrated promise in pilot study. An additional strength is that we will be examining mediators to identify potential barriers to stigma reduction (e.g., depressive symptoms, substance dependence). We will also use a stepped wedge technique to maximize power and collect data in a time- and resource-efficient manner.

3h. Dissemination of Findings. We have already presented pilot study findings at invited lectures and national conferences.[76,134] We plan to continue to submit and present findings for relevant national and international conferences (United States Conference on AIDS, Joint Symposium on HIV Research and Women, International AIDS Conference, etc.). In addition, we plan to submit several manuscripts on this study. Four planned manuscripts include "Effectiveness of a Stigma Reduction Intervention for African American Women Living with HIV," "Stigma Reduction and Its Impact on Health Outcomes for African American Women Living with HIV in Chicago and Birmingham." Publication of intervention results will follow the modified CONSORT guidelines.[135]

3i. Future Studies. If effectiveness of the Unity Workshop to reduce internalized stigma is established, future studies may focus on the cost-effectiveness of reducing stigma using this brief workshop given in the clinic setting. Future work may also explore the value of stigma reduction programs for preventing the emergence of depressive and anxiety symptoms and substance-dependence among PLWH.