Development and evaluation of a theory-informed mHealth intervention to promote viral suppression among women living with HIV who engage in sex work in Mombasa, Kenya: the role of text messaging, social support and stigma

Frances M. Aunon

A dissertation

Submitted in partial fulfillment of the
Requirements for the degree of

Doctor of Philosophy

University of Washington
2020

Reading Committee:
Jane Simoni, Chair
William George
Scott McClelland

Program Authorized to Offer Degree:
Department of Psychology

University of Washington

Abstract

Development and evaluation of a theory-informed mHealth intervention to promote viral suppression among women living with HIV who engage in sex work in Mombasa, Kenya: the role of text messaging, social support and stigma

Frances M. Aunon

Chair of the Supervisory Committee:
Jane M. Simoni
Department of Psychology

HIV is a global pandemic exacting a disproportionate burden on sub-Saharan Africa. A key population affected by HIV are women who engage in sex work. Effective antiretroviral therapy (ART) has revolutionized HIV treatment and prevention, yet strict adherence remains a barrier to achieving viral suppression. Mobile health (mHealth) interventions have been evidenced to improve ART adherence and viral suppression. HIV-related stigma is pervasive, especially in conjunction with the stigma of sex work. There is evidence that social support may buffer the effects of stigma on poor adherence and HIV treatment outcomes. However, current research on social support and stigma is limited by an individual focus. Social network analysis is an increasingly popular methodology utilized to overcome this shortcoming and more accurately describe the environment in which persons of interest interact. The aims of this dissertation are: 1) to develop a theory-informed, mHealth intervention to improve ART adherence and viral suppression among women who engage in sex work in Kenya, 2) to evaluate the efficacy of the intervention to improve ART adherence and viral suppression in a randomized controlled trial, and 3) to leverage social network analysis to examine the relative impact of HIV-related stigma and social support on viral suppression. Focus groups with women who engaged in sex work informed the content and structure of the mHealth intervention, entitled *Motivation Matters!*.

When compared to an active standard of care condition, women receiving *Motivation Matters!* endorsed higher rates of ART adherence and viral suppression, especially among women who were viremic at baseline and reported engagement in sex work. Finally, although we did not find significant relationship between individual and network-level measures of stigma and social support on viral suppression, further examination of the women's social networks suggested that the experience of stigma had a more significant impact on viral suppression. In conclusion, the improvements in ART adherence and viral suppression suggests that *Motivation Matters!* could be an effective tool to support the treatment of women living with HIV in sub-Saharan Africa. Moreover, utilizing social network analysis provides a more rich and in-depth depiction of the social topography of women living with HIV, which could open doors for researchers to develop more effective interventions to support the women's health and wellbeing.

Table of Contents

Acknowledgements

I would like to thank the University of Washington STD & AIDS Research Training Program (NIH T32AI07140) for generously supporting my education and providing outstanding training and mentorship from such supportive and dedicated faculty.

I would like to thank my committee, Dr. Jane Simoni, Dr. William George, Dr. Shannon Dorsey, Dr. Scott McClelland, and Dr. Chris Adolph. I especially want to thank Dr. Jane Simoni for her commitment to mentorship and steadfast support throughout these last five years.

I would like to thank the Simoni Lab, especially Dr. Bryan Kutner, PhD, MPH, Dr. Joyce Yang, PhD, Megan Ramaiya, MPH, and Liying Wang for their consistent positive reinforcement, pep talks, and accountability. I thank my cohort for their continued camaraderie. I would also like to thank my research assistants, Emma Creegan and Cameron Casey for their reliable support. I thank the CSSS and CSSCR statistical consultants for their patience and guidance. I thank Jeanny Mai and the rest of our UW colleagues, especially Dr. Corey Fagan and Dr. Ron Smith, for promoting such a collegial and caring department culture.

I would like to extend my gratitude to my counterpart in Mombasa, George Wanje, MPH, and the rest of the team of doctors, nurses, administrators at the Ganjoni Clinic in Mombasa, Kenya. This study would not have happened without you.

In addition, I would like to thank my parents, Alfredo and Mary Aunon, my brother, Andrew Aunon, sister-in-law, Dana Aunon, and partner, Andrew Simon, as well as the whole host of aunts, uncles, cousins, who keep me grounded. Lastly, I would like to thank the friends who have become family for their unconditional support – I could not have gotten here without you.

Dedication

To the study participants who risked sharing their experience for the betterment of others and to the study team, without which this study would not have been possible.

Chapter I.

Introduction

In 2015, there were an estimated 36.7 million people living with HIV (PLWH) (UNAIDS, 2016a). HIV prevalence is not uniform across the globe; sub-Saharan Africa, in particular, is the region hardest hit by HIV. Although it represents only 10% of the world's population, it contains nearly 70% of the global population of PLWH or 25.5 million individuals (UNAIDS, 2016d). The demography of the HIV epidemic in sub-Saharan Africa differs compared to the rest of the world. Women are disproportionately affected by HIV in the region, accounting for 59% of new HIV infections of adults, compared to 47% globally.

Globally, women who engage in sex work and their clients account for approximately 10% of new HIV infections (UNAIDS, 2016c). Recent meta-analyses estimate that HIV prevalence rates among women who engage in sex work in sub-Saharan Africa range from 31% to 37% (Baral et al., 2012; HIVAIDS, 2014). Women living with HIV who engage in sex work have a higher number of sexual partners compared to women of reproductive age from the general population, which increases the likelihood of HIV acquisition as well as HIV transmission to sexual partners (Baral et al., 2012). In Kenya, women who engage in sex work represent about 1% of the population, yet contribute to approximately 14% of new HIV infections (National AIDS Control Council, 2012).

The advent and dissemination of antiretroviral therapy (ART) has transformed HIV infection from a terminal disease to a manageable chronic illness (U S Department of Health and Human Services & AIDS, n.d.). ART effectively suppresses the HIV RNA viral load which virtually eliminates the risk of HIV transmission (Bangsberg, 2006; World Health Organization, 2012). If everyone living with HIV were virally suppressed, HIV transmission would cease and the HIV epidemic would be eliminated (Dodd, Garnett, & Hallett, 2010; Granich, Gilks, Dye, De Cock, & Williams, 2009). However, achieving viral suppression depends on maintaining

consistently high levels of ART adherence (Palmisano & Vella, 2011; Vella, Schwartländer, Sow, Eholie, & Murphy, 2012).

Improving ART adherence and viral suppression among women who engage in sex work may prevent forward transmission of HIV (World Health Organization, 2012), however they can be a difficult population to treat. A meta-analysis summarizing nine studies worldwide found that only 57% of women living with HIV who engage in sex work and were taking ART achieved viral suppression (Mountain et al., 2014). Additional research in Kenya echoes these global findings; engagement in sex work was associated with a twofold decrease in ART adherence (Mukui et al., 2016). These findings highlight the need for more targeted interventions to address barriers to ART adherence and viral suppression.

Socio-ecological theory provides a framework for understanding barriers to ART adherence. The theory organizes factors influencing behaviors at intersecting levels, suggesting that stigma and social support influence ART adherence not only at the *individual* level, but also at the *interpersonal* level (e.g., via experiences of stigma and exchanges of support) and the *community* level (e.g., via stigmatizing and supportive norms; Bogart, Cowgill, & Kennedy, 2008; Gilbert & Walker, 2010). However, current research on social support and stigma is limited by an individual focus (Holzemer et al., 2007). Social network analysis may provide a mechanism and methodology to more accurately understand how support and stigma at the interpersonal level influence ART adherence.

Through my dissertation, I attempted to better understand the barriers and facilitators to ART adherence, with the ultimate aim of improving rates of viral suppression, among women living with HIV in Mombasa, Kenya. My dissertation data come from an NIMH-funded study

(NIMH R21 MH107217, PI: McClelland, co-I: Simoni). I served as the study coordinator and facilitated all components of the study planning, implementation, and analysis.

The first aim of my dissertation involved the development of a theory-informed, mobile health ("mHealth") intervention, entitled *Motivation Matters!*, which aimed to improve viral suppression among women living with HIV in Mombasa, Kenya. I present findings from the focus group discussions with women living with HIV who engage in sex work that informed the content and structure of *Motivation Matters!*.

Second, in order to better understand how an individual's interpersonal context influences viral suppression and address the gaps in the literature about factors influencing ART adherence beyond the individual level, I collected egocentric network data to examine how social support and stigma influence behavior at the interpersonal level. These data allow me to examine the relative impact of stigma and social support on viral suppression.

Finally, my third aim presents the outcome of the randomized controlled trial assessing the efficacy of the *Motivation Matters!* intervention developed in my first aim. In addition to discussing the primary intervention effect on viral suppression and ART adherence, I also examined the feasibility and acceptability of the intervention.

It is my hope that these data will allow us to identify more innovative and effective strategies for improving ART adherence and viral suppression among women living with HIV in sub-Saharan Africa.

References

Bangsberg, D. R. (2006). Less Than 95% Adherence to Nonnucleoside Reverse-Transcriptase Inhibitor Therapy Can Lead to Viral Suppression. *Clinical Infectious Diseases*, *43*(7), 939–941. http://doi.org/10.1086/507526

Baral, S., Beyrer, C., Muessig, K., Poteat, T., Wirtz, A. L., Decker, M. R., et al. (2012). Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. *The Lancet Infectious …*, *12*(7), 538–549. http://doi.org/10.1016/S1473-3099(12)70066-X

Bogart, L. M., Cowgill, B. O., & Kennedy, D. (2008). HIV-related stigma among people with HIV and their families: A qualitative analysis. *AIDS and Behavior*, *12*, 244–254.

Gilbert, L., & Walker, L. (2010). "My biggest fear was that people would reject me once they knew my status…": stigma as experienced by patients in an HIV/AIDS clinic in Johannesburg, South Africa. *Health & Social Care in the Community*, *18*(2), 139–146. http://doi.org/10.1111/j.1365-2524.2009.00881.x

Holzemer, W. L., Uys, L. R., Chirwa, M. L., Greeff, M., Makoae, L. N., Kohi, T. W., et al. (2007). Validation of the HIV/AIDS Stigma Instrument—PLWA (HASI-P). *AIDS Care*, *19*(8), 1002–1012. http://doi.org/10.1080/09540120701245999

Mountain, E., Mishra, S., Vickerman, P., Pickles, M., Gilks, C., & Boily, M.-C. (2014). Antiretroviral Therapy Uptake, Attrition, Adherence and Outcomes among HIV-Infected Female Sex Workers: A Systematic Review and Meta-Analysis. *PLoS One 9*(9), e105645. http://doi.org/10.1371/journal.pone.0105645

Mukui, I. N., Ng'ang'a, L., Williamson, J., Wamicwe, J. N., Vakil, S., Katana, A., & Kim, A. A. (2016). Rates and Predictors of Non-Adherence to Antiretroviral Therapy among HIV-

Positive Individuals in Kenya: Results from the Second Kenya AIDS Indicator Survey, 2012. *PLoS One*, *11*(12), e0167465. http://doi.org/10.1371/journal.pone.0167465

National AIDS Control Council. (2012). *Kenya AIDS epidemic update 2011*. Nairobi, Kenya.

U S Department of Health and Human Services, & AIDS (n.d.). *A Timeline of HIV/AIDS*. Retrieved from https://www.aids.gov/hiv-aids-basics/hiv-aids-101/aids-timeline/

UNAIDS (2016a). *AIDS Info*. Retrieved from http://aidsinfo.unaids.org/

UNAIDS (2016b). *Fact Sheet November 2016*. Retrieved from http://www.unaids.org/en/resources/fact-sheet

UNAIDS (2016c). *Global AIDS Update 2016*. Geneva. Retrieved from http://www.who.int/hiv/pub/arv/global-AIDS-update-2016_en.pdf?ua=1

UNAIDS (2016d). *Prevention Gap Report*. Retrieved from http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf

World Health Organization. (2012). *Antiretroviral Treatment as Prevention (TasP) of HIV and TB: 2012 update*. Geneva. Retrieved from http://apps.who.int/iris/bitstream/10665/70904/1/WHO_HIV_2012.12_eng.pdf

Chapter II:

Development of a nurse-delivered mHealth intervention to support treatment adherence among women living with HIV who engage in sex work initiating or switching antiretroviral therapy in Mombasa, Kenya

Abstract

Background: Nurses have an integral role to play in achieving UNAID's 95-95-95 goals to stem the HIV epidemic. In this paper, we used the Information-Motivation-Behavioral Skills (IMB) theoretical model to develop a nurse-delivered, mHealth intervention to support ART adherence among women living with HIV who engage in sex work in Mombasa, Kenya.

Methods: Twenty-three purposively sampled women living with HIV who engage in sex work participated in five focus group discussions (FGDs) to iteratively develop the message content as well as the format and structure of the nurse-delivered, text-based intervention. FGD interview guides were developed in accordance with the IMB model. Transcripts were analyzed according to IMB themes and findings were used to develop the intervention.

Results: Information-oriented texts addressed concerns and misconceptions. Motivation-oriented texts reinforced women's desires to feel healthy enough to engage in activities, and behavioral skills-oriented texts included strategies to remember ART doses.

Conclusion: The nurse-delivered, theory-based, culturally-tailored intervention to support ART adherence is currently being evaluated.

Introduction

Women who engage in sex work bear a disproportionate burden of HIV infection and have been identified as a key population for HIV prevention (Garrett et al., 2017). Improving HIV prevention and treatment support to key populations is necessary to achieve the Joint United Nations Programme on HIV/AIDS 95-95-95 goals and stem the HIV epidemic (Sanne et al., 2010; UNAIDS, 2016). In Kenya, women who engage in sex work represent approximately 1% of the population and 5% of women of reproductive age, yet account for over 14% of new HIV infections (Odek et al., 2014; UNAIDS, 2013). Antiretroviral therapy (ART) is highly efficacious for reducing morbidity, mortality, and the risk of transmission of HIV (Cohen et al., 2016; Granich, Gilks, Dye, De Cock, & Williams, 2009; Richman, 2018). However, the success of treatment requires high levels of adherence (Bangsberg et al., 2001; Haberer et al., 2017). A recent review found that 76.2% of women who engage in sex work from low- and middle-income countries reported adequate levels of ART adherence (CI:67.8-83.0) (Mountain et al., 2014). Social and structural barriers may limit women's ability to adhere to ART, highlighting the need for interventions directly supporting adherence in this key population (Mountain et al., 2014). Few interventions have been developed with the input of women who engage in sex work. Rather, the majority were developed for other populations and later adapted (Moore et al., 2014). Some research suggests women who engage in sex work do not respond as well to current HIV prevention interventions targeted to the general population (Mountain et al., 2014).

Mobile health (mHealth) interventions have been identified as an innovative approach to facilitate ART adherence and viral suppression. Two early mHealth interventions found that text messages can improve rates of viral suppression among people living with HIV (Lester et al., 2010; Pop-Eleches et al., 2011). While the initial mHealth studies were promising, recent

evidence has been more mixed, with some studies showing a benefit to ART adherence and others showing no impact of mHealth interventions (Linnemayr et al., 2017; Shet et al., 2013).

Incorporation of a theoretical framework may influence intervention efficacy (Bull & Ezeanochie, 2015). Health behavior theories can help explain the mechanisms through which an intervention is effective and evidence suggests that interventions developed according to a theoretical framework may be more efficacious than interventions developed without a theoretical framework (Chi & Stringer, 2010). While many mHealth interventions have cited a theoretical framework (Simoni, Aunon, & Ronen, 2018), only a few have provided a detailed description of how the health behavior theory was integrated throughout the development and implementation of the intervention (Hall, Cole-Lewis, & Bernhardt, 2015; Michielsen, Chersich, Temmerman, Dooms, & Van Rossem, 2012; Odeny et al., 2014).

In the absence of a clearly defined theoretical framework for the initial studies demonstrating the efficacy of mHealth interventions in improving ART adherence (Lester et al., 2010), it is necessary to understand the mechanisms through which the interventions effectively influenced ART adherence. One such hypothesis is that the text messages may have functionally motivated ART adherence (Hall, Cole-Lewis, & Bernhardt, 2015). Thus, interventions aiming to improve motivation may be more efficacious than interventions that do not leverage motivation.

The Information-Motivation-Behavioral Skills (IMB) theoretical framework is one model used to explain HIV risk and ART adherence (Ajzen & Fishbein, 1980; Bandura, 1994; Fisher & Fisher, 2000; Starace et al., 2006). One aspect that differentiates the IMB theoretical framework from other health theories is the emphasis placed on motivation as a determinant of behavior (Fisher & Fisher, 1992). A recent meta-analysis of qualitative studies highlighted the importance of interpersonal connections in adhering to ART; out of all of the tiers in Maslow's hierarchy of

needs, the “love and belongness” tier was the tier with the strongest connection to ART adherence (Barroso, Leblanc, Flores, 2017). We hypothesize that successful interventions improve adherence by enhancing motivation to take ART because text message recipients feel cared for by the nurses. The intervention will also allow nurses to provide information and coaching on behavioral skills to support adherence.

Given the scarcity of interventions developed by and for women living with HIV who engage in sex work and the lack of literature detailing the development of mHealth interventions, this paper presents the intervention development study of the *Motivation Matters!* Intervention that used qualitative methods. Guided by the IMB theoretical framework, the intervention was iteratively informed by women living with HIV who engage in sex work who we hope will benefit from the intervention. This interactive text message-based intervention to support medication adherence in women who engage in sex work who are initiating or changing ART regimens was conceptualized in accordance with IMB theory.

Methods

Three qualitative focus group discussions (FGDs) were conducted with women living with HIV who engaged in sex work who were engaged in care at the Ganjoni Clinic in Mombasa, Kenya. The women living with HIV were purposively selected to include those who were and were not currently taking ART. Women were all over 18 years old and had individually consented to participate in FGDs with other women living with HIV who engage in sex work.

The purpose of the FGDs was to identify themes to inform development of the nurse-delivered mHealth intervention to improve ART adherence and viral suppression. Following the IMB model, FGDs were structured to identify *information* and misconceptions that may

influence adherence (including common perceptions of ART and sources of information related to ART), highlight sources of *motivation* (including sources of motivation and perceptions of clinic staff), and elicit effective *behavioral skills* that impacted ART adherence (including common adherence challenges and responses). The facilitators for the FGDs also solicited feedback about the feasibility of the intervention, including the acceptability of sending intervention messages to cell phones, recommendations for the frequency and timing of message delivery, and concerns about confidentiality. The FGD interview guide was developed in collaboration with the clinic staff and nurses prior to implementation.

All FGDs were facilitated by a Kenyan social scientist with experience in qualitative interviewing and focus group facilitation and were held in a private room at the Ganjoni Clinic. The groups were stratified by ART status and included one FGD with ART-naïve women and two FGDs with women on ART. Women were grouped by ART use to ensure that concerns of treatment-naïve patients were incorporated in addition to the perspectives of women already on treatment. All FGDs were audio recorded, transcribed, and translated. Transcriptions were reviewed by author GW who is fluent in the local language and compared with the audio recordings to ensure there was no loss of meaning through translation. To protect the women's anonymity, names were not included on any of the digital recordings or transcripts. All data were stored on encrypted and password protected computers and servers.

Transcripts were uploaded and analysed using Atlas.ti 7.5.2 (Muhr, et al, 2012). Authors GW and FMA coded and analysed the data using a directed approach according to the IMB model (Hsieh & Shannon, 2016). Sub-themes were identified within the information, motivation, and behavior skills constructs (Corbin & Strauss, 2008). Common concerns, misconceptions, and recommendations expressed by participants in the FGDs informed the study team's initial

development of text message content, personalization, and structure. All text messages were related to themes of information, motivation, and behavioral skills surrounding ART adherence.

Following the initial drafting of the text messages by the study team, women from the first three FGDs were invited back twelve weeks later to review the content in two follow up FGDs. During these follow up FGDs, facilitators presented text messages on large poster board and edited messages based on the women's feedback, emphasizing clarity, relevance, and acceptability. Given the highly interactive and conversational nature of these discussions, these two FGDs were not transcribed or translated (Simoni et al., 2019).

All research procedures were approved by the Human Subjects Research Committee of the University of Washington, Seattle, USA and by the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee in Nairobi, Kenya. All participants provided written informed consent and were reimbursed KSh 250 (approximately $2.50 USD) at each FGD for their transportation costs and time.

Candidate's contributions

As study coordinator, Ms. Aunon collaborated with the study to outline the questions FGD guides, and incorporate the feedback from the FGDs into the design of the intervention. She conducted the qualitative data analysis with colleagues George Wanje and Elena Okada and took the primary role in writing the manuscript.

Results

A total of 23 women participated in three FGDs to inform content development for the first draft of text messages for the nurse-delivered mHealth intervention; 17 of the women returned to review the content of the text messages in two follow-up FGDs. Their median age

was 46.2 years (interquartile range [*IQR*] 40.5-50.0), and they had a median of 7.0 years of education (*IQR* 5.5-9.0). Sixteen women (70.0%) were taking ART, with a median of 6.0 years (IQR 3.8-9.0) on treatment. The majority of women were Christian (*n*=22, 95.7%). Most were either widowed or divorced (*n*=18, 78.3%).

Paralleling the structure of the FGDs, results are organized by the themes of information, motivation, and behavioral skills. These thematic sections are followed by a summary of the women's feedback regarding the feasibility of the nurse-delivered mHealth intervention. The final section of the results explains how the intervention was structured based on the feedback from the FGDs.

Information about and attitudes towards ART

Women were asked to highlight common attitudes toward ART and identify any personal or community concerns about treatment. While women recognized that community members were taking ART to manage HIV, they expressed *differing opinions about whether taking ART was healthy*. One woman shared, "There are a number of people in the community who know about these drugs, and they also understand that when one uses these drugs they become healthier. [However,] some people say that when you use ART, HIV becomes worse" (34 years, ART for 3 months). These conflicting beliefs were echoed by ART-naïve women. One woman shared, "I can see [ART] is doing [my sister] good because she is healthy" (29 years, ART-naïve). In contrast, another woman said, "I have personally seen someone who is using [ART] and that person is suffering…every time she was given those drugs her [blood] pressure went up" (45 years, ART-naïve).

Some women highlighted *safety concerns of long-term ART use and potential adverse effects*. While a number of women expressed concepts like, "ART is for life; when you start there is no stopping," (46 years, ART for 4 years), many shared a belief that ART was only effective for a limited period and warned against long-term use. "If you use ART longer than fifteen years, then you will die… I heard some people in the community say that if you use those drugs for a long time, your liver gets exhausted" (56 years old, ART for 6 years). ART-naïve women echoed concerns about potential adverse effects of ART. "There are many side effects [of ART]. You might have itching skin or develop thorn-like things on your body. Others might have burnt skin or become blind" (45 years old, ART-naïve).

Despite concerns about the potential adverse effects of ART, many women *recognized the value of ART adherence*. One woman noted that missed doses may contribute to virus replication. "It is important to take the drugs…When you start to skip, the virus becomes strong again and starts to multiply," (52 years, ART for 6 years). While women understood the need to take ART consistently, there was confusion regarding how to handle a missed dose. Some women reported taking a missed dose as soon as they remembered – "[I was] supposed to take my drugs at 7am or 8am. I remembered at 10am and took my drugs," (41 years, ART for 6 years). Others thought they were supposed to skip a dose if they forgot to take it on time. "I was told that if you forget the drugs, you leave it like that. You don't take them. You go on with the next dose," (49 years, ART for 10 years). One ART naïve woman highlighted that "stress builds up" and could contribute to forgetting to take ART: "Sometimes you could be having a problem, your status is not as you want it to be, and sometimes you do not even have money for basic needs which makes you becomes stressed until you forget to take medicine," (45 years old, ART-naïve).

Several misconceptions were shared about the perceived *detrimental effects of ART and alcohol consumption*. Many women questioned the effectiveness of ART when combined with alcohol and some women said they were advised to "avoid alcohol" altogether (52 years, ART for 6 years): "I was taught that when one takes alcohol it washes away the drugs from the body because of urinating frequently," (56 years old, 10 years on ART). Other women believed that alcohol would not only render ART ineffective, but could also cause significant harm: "Taking ART and drinking alcohol concurrently, especially if you took the dose first then drink alcohol, means the drug will not work. When you use drugs and alcohol it spoils your liver and kidneys, because alcohol and drugs are a dangerous combination," (34 years, ART for 3 months). Another common narrative was that alcohol could contribute to forgetting to take ART: "When you are on medication and take alcohol, you can forget [to take ART]. By the time you remember, the alcohol content is higher than the drug and thus gives the virus an opportunity to multiply," (47 years, ART for 9 years).

Some women turned to *traditional medicine and religion as alternatives to ART*. One theme that emerged as a reason for choosing traditional medicine over ART was the desire to avoid inadvertent disclosure of HIV status. "Most of the time what makes us not take ART is the use of herbal medicine. [Instead of taking ART,] we boil the herbal medicine because we are afraid that our family members will find out about our [HIV] status," (38 years, ART for 9 years). While some community members use traditional medicine, one woman added, "[but] then, you will hear they died," (49 years, ART for 10 years). Women shared that, "people who [falsely] say they are doctors" spread skepticism about the effectiveness of drugs, saying, "if you take [ART] your body slowly deteriorates," (56 years, ART for 6 years).

Women shared that some community members' *persistence of religious beliefs* contributed to their decision to stop taking ART. While faith provided a source of hope, both ART-experienced and ART-naïve women shared stories of friends who died because they felt God cured them of HIV, leading them to discontinue ART: "My friend went to church and they prayed and prayed. She defaulted [on her ART] because she believed that she was healed. We have already buried her. It is true that this disease is real and God is also real," (38 years, ART for 9 years). One woman warned against ignoring a health provider's instructions: "If the doctor has not instructed you to stop your medication and you stop and say that God is with you, you will die," (52 years, ART-naïve).

Motivation to adhere to ART

Women were asked to describe what encouraged themselves and others to take ART, and factors that might affect motivation for adherence. Many women recognized how ART allowed them to *re-engage in everyday activities* and feel "like a normal person" again (47 years, 9 years on ART). One woman explained, "If I take these drugs like I am supposed to, I can do any work. I have clearly seen the benefit of these drugs," (56 years old, ART for 6 years). This return to normalcy continued to motivate their own adherence: "Many times we lose hope when we know that we are positive…but taking these drugs makes you understand that you still have days to live in future so you can live without doubts again like other people," (47 years, 9 years on ART).

Most women felt *supported by health care providers*, which motivated them to take ART and stay engaged in care. One woman shared how the positive rapport with providers gave her hope. "The encouragement and teaching [from the clinic] is very good. They prevent you from

worrying and losing hope. Any provider you talk with encourages you and raises your spirits. It's a good thing," (47 years, ART for 9 years). Trusting health care providers' intentions was helpful among ART-naïve women, allowing them to accept their HIV diagnosis and increase their confidence in providers' recommendations. "Sometimes we are bothered by our diagnosis and question whether it is true. However, we know the doctor wants to help us," (45 years, ART-naïve). The women specifically highlighted the role nurses played in increasing their motivation to start ART: "The nurses are the ones who convinced me to start [ART]. I had completely refused, [but] they gave me facts and completely convinced me [to start ART]" (46 years, ART for 4 years). Many women described how talking with nurses decreased their hopelessness by providing support and education. "[The nurses] give us encouragement and teaching such that we do not worry or lose hope…It's a good thing" (47 years, ART for 9 years).

The *value of families and loved ones* were significant sources of support and motivation for ART adherence. "I feel happy that other people support me. The other day, my sister called me to check on me. I felt cared for," (40 years, ART-naïve). For some women, partners provided support for ART adherence. One women added, "My husband reminds me to take my medication. When I forget, he goes and picks them up for me," (40 years, ART for 1.5 years). Many mothers shared how the desire to stay alive for their children motivated treatment adherence: "I look at my children and think that if I die [from not taking ART], I will leave them orphaned. It's better to take the medication so that I may take care of them," (46 years, ART for 4 years).

Women also expressed faith that *God would take care of them*, but emphasized the continued need to take medication. One woman explained:

> "We don't have a choice [about taking ART]… until God comes down and uses his people to manufacture medicine to treat it completely. We take [ART] while praying to God to give us his grace to get a cure, but we cannot stop taking the medicine," (56 years, ART for 10 years).

Behavioral skills that impact adherence

Women shared barriers, *like the logistics of taking ART and having routines disrupted by travel*, that could impact ART adherence as well as strategies to overcome them. Many ART-experienced women reported taking their medications consistently, and shared strategies they used to support adherence. One woman stated,

> "You don't have to carry a purse to carry your drugs. You are a woman with breasts and wear a bra, place them there. If you are wearing underwear, put them there. When the time comes [to dose], you excuse yourself and take your drugs and the day goes on," (47 years, ART for 9 years).

Changes in routine presented a barrier to ART adherence. Many women on ART shared how they would plan ahead for travel to ensure consistent adherence. "If you know that you are going to travel, take your medicines with you because you don't know what will happen ahead," (40 years, ART for 1.5 years).

The women described the importance of *asking health care providers questions* when they had concerns about ART. Several women experienced adverse effects, especially upon treatment initiation. One woman explained how her adverse effects were easily resolved when she discussed her concerns with her health care provider. "When I started taking these drugs, I started itching on the second day. When I came back here [I talked with the health care provider]

and I had my drugs changed," (52 years, ART for 6 years). Another woman described how visiting the clinic helped her manage her ART adverse effects:

> "After a month of starting ART, my feet started losing sensation. I visited the nurse and she explained that it would stop. And true to her word, over time, the sensation in my feet returned and I became well. I am doing fine," (34 years, ART for 3 months).

Intervention Feasibility

In addition to ascertaining how information, motivation and behavioral skills influenced ART adherence, researchers conducting the FGDs solicited the women's suggestions for designing a nurse-delivered mHealth intervention that was feasible. Participants were asked about the availability of cell phones and literacy rates in the community. In addition, women shared preferences regarding text message frequency and concerns about confidentiality. Finally, they provided feedback for the proposed text message response options and message personalization. This information informed the development of a nurse-delivered mHealth intervention to improve ART adherence that we hope will be acceptable, accessible, and appropriate for women in Mombasa, Kenya.

While the research team was concerned about the ubiquity of *phone ownership* among such a low income target population, women assured us that, "right now, everyone has a phone…You will find even my grandmother has a phone back at home," (46 years, ART for 4 years). Additionally, women felt confident that literacy would not prevent the comprehension of text messages. One woman stated, "Even a nursery school child knows how to read Kiswahili," (40 years, ART-naïve). Should any questions arise, women suggested a trusted confidant, such as their children, may be able to help with reading: "My son would help me if I couldn't read

them," (38 years, ART for 9 years).

Women had differing opinions regarding the desired *frequency of text messages*. While some women requested messages several times a day – "It can be easy to forget taking your drugs at the correct time. [Therefore,] we should be reminded two times a day," (45 years, ART-naïve), others suggested less frequent messages: "Two times a week is okay, but two times a day!... It will cause problems with your husband," (29 years, ART-naïve). While strong opinions were expressed for a range of frequencies, most women felt that 2-3 messages per week would be reasonable during the first two months, reducing the frequency to one message per week in later months. In addition, women requested the flexibility for messages to be sent "at the individual's preferred time" to ensure privacy (47 years, ART for 9 years).

Almost all of the women expressed *concerns about confidentiality,* given the potentially sensitive nature of the content in the messages. The women recommended that messages avoid using words that may inadvertently disclose their HIV status. "Most of us fear that word, 'ART.' That word should not be seen [in the text messages]. Use any other word instead so that people who come across her text messages don't know that she's HIV-positive," (49 years, ART for 7 years). Women suggested referring to HIV as less stigmatized medical conditions, such as malaria or blood pressure: "The text messages could instruct us to take medication and sleep under a net. Your spouse would think the texts related to malaria prevention and would not know you are on ART," (47 years, ART for 9 years).

In addition to concerns about inadvertent disclosure, some women suggested that a women, and especially a nurse, send the text messages to avoid their partner's suspicion. As one woman stated, "Men are jealous; they may become suspicious" and recommended, "if the message is sent from a female's number, it will save us a lot of trouble," (41 years, ART for 6

years). Another woman added that, “If it is possible, [the text messages] should be sent by Sister Carol’s number. Even if someone else sees the message, they can call the number…there will be no problems” (29 years, ART-naïve). The women suggested that they “[felt] good” about the nurses sending the messages as it would “boost morale,” and “improve motivation and increase faith in the clinic staff” (47 years, ART for 9 years).

Intervention Development

Based on qualitative data from the first three FGDs, the research team developed text messages to promote ART adherence. These messages were then shared with women in two additional FGDs to ensure that the study team interpreted their feedback accurately. Example text messages, organized by IMB themes, can be found in Table 1. The complete set of text messages is available as supplemental digital content. Based on the women’s feedback, the study team *personalized* text messages by name, family status (children or not), language, religion, and the time of day the messages are sent. For example, for Christian women, texts could close with “Be blessed,” while texts for Muslim women could open with traditional Arabic greetings such as “As-salamu alaykum,” (peace be upon you). All text messages were signed from “Sister Carol,” one of the nurses at the clinic; “sister” is a common way to address nurses in Kenya.

For the planned randomized controlled trial (RCT), it was important that women receiving messages confirmed receipt. The study team suggested that women respond with “poa,” meaning well or okay, and “swali,” meaning question, the responses utilized in prior research (Lester et al., 2010). If a study participant indicated that they had a question or did not respond, they would receive a call from study staff within 24 hours. These text responses and call backs were considered acceptable by the women in the FGDs, but there was some concern about

the cost of sending replies. To address this issue, the RCT protocol was designed to provide airtime to cover the cost of sending the replies.

Over the course of the 6-month intervention, a quarter of the messages were designed to provide information, half related to motivation, and a quarter addressed behavioral skills. Given the many misconceptions about ART that were shared during the FGDs, the study team included a higher proportion of information-oriented text messages during the first six weeks of the intervention. In addition, in response to the women's feedback, messages were sent with a higher frequency during the first two months of the intervention period (2-3 text messages per week), with the frequency declining to 1-2 messages per week thereafter. To address the women's concerns about confidentiality, the study team avoided all HIV-related terms in the text messages, referring to ART as "blood pressure medication." Finally, text messages were signed from a female nurse, and the women receiving the intervention were to be counselled to save the number under a female name to minimize potential tension with partners.

Discussion

This paper describes the use of qualitative FGDs to generate content for an IMB-informed, nurse-delivered mHealth intervention to promote ART adherence among women who engage in sex work in Mombasa, Kenya. The FGDs revealed both accurate and inaccurate information about ART. There was a general understanding that ART must be taken consistently, but many members of the community expressed concerns about the safety of treatment. This ambivalence about the risks versus benefits of ART contributed to some community members turning to traditional medicine and faith healing as alternatives to ART. Several factors were strong motivators supporting ART use. Regaining the ability to engage in everyday activities and

feeling supported by health providers motivated ART adherence and generated hope for the future. In addition, women reported feeling powerfully motivated to adhere for the sake of surviving to care for their children. Finally, women shared behavioral strategies to support taking medication, including creative reminders for taking ART and asking health providers when they encountered questions. Drawing from the IMB themes in the FGD data, text messages were developed and tailored for the *Motivation Matters!* intervention.

The structure of the intervention was developed based on women's feedback regarding acceptability, and informed by best practices from the mHealth intervention literature (Hall et al., 2015). Consistent with global trends identified by the World Bank (Qiang, Yamamichi, Hausman, & Altman, 2011), the women affirmed that cell phone access was virtually universal in this community. While some women requested more frequent text messages as 'reminders' to take ART, the mHealth literature suggests that daily text messages may be less effective (Hall et al., 2015; Horvath, Azman, Kennedy, & Rutherford, 2012), with burnout increasing over time. Thus, *Motivation Matters!* was designed with 2-3 messages per week during the first six weeks, then 1-2 messages per week for the remainder of the 6-month intervention period. Fear of HIV disclosure was a common concern among women in the FGDs and has been echoed among people living with HIV in a wide range of settings (Evangeli & Wroe, 2016). Consistent with several HIV-related mHealth interventions (Katz et al., 2013), the *Motivation Matters!* intervention content was designed to avoid any HIV-related verbiage to reduce the potential of inadvertent disclosure. In addition, to minimize possible suspicion from potentially jealous male partners, the intervention includes the recommendation that women save the study messaging number in their phone under a woman's name.

Several mHealth studies have suggested that personalized messages have a greater impact on ART adherence compared to non-personalized messages (Finitsis, Pellowski, & Johnson, 2014; Horvath et al., 2012; Park, Howie-Esquivel, & Dracup, 2014), but few interventions have personalized message content based on multiple factors. Participants in the FGDs that informed the development of the *Motivation Matters!* intervention favored personalization based on name, family status (children or not), language, religion, and the time of day the messages are sent. Finally, the intervention was designed to be interactive, by incorporating bidirectional text messaging. A recent meta-analysis of mHealth interventions suggested that bidirectional, messaging was more effective at improving ART adherence compared to one-way texts (Finitsis et al., 2014). In addition to promoting increased engagement in the intervention, the bidirectional texting incorporated in the *Motivation Matters!* intervention is intended to support confirmation of message receipt and allow women who have questions regarding their care to request a call back from a nurse. This increased communication with nurses is intended to improve the patient-provider relationship (supporting motivation), and to provide easy access to correct information about ART, both of which may lead to improved treatment adherence (Brion, 2014).

This intervention development had a number of important strengths. First, *Motivation Matters!* was developed through an iterative process where the IMB theoretical framework guided the incorporation of both the FGD participants' feedback and findings from current research, which may facilitate greater understanding of the mechanism impacting ART adherence. Moreover, the use of a well-established behavioral theory could support future translation of the intervention to other mHealth platforms as technology evolves (Muessig, LeGrand, Horvath, Bauermeister, & Hightow-Weidman, 2017; Riley et al., 2011; Simoni et al., 2018). Second, the structure of the intervention in terms of timing, frequency, and

bidirectionality, were informed by a growing body of literature on what works in mHealth interventions for adherence to health behaviors. Third, the content and structure of the *Motivation Matters!* intervention were developed by and designed for women who engage in sex work, a key population disproportionately affected by the HIV epidemic. This research included both formative FGDs and follow-up FGDs to validate the study team's interpretation of the data and allow participants to directly revise and fine-tune the intervention content and structure. Fourth, the *Motivation Matters!* intervention attempts to address the identified need for interpersonal connection by increasing the contact the women have with clinic staff through both the messages and the motivational message content. Finally, the intervention utilizes a task shifting approach utilizing nurses, which may contribute to more sustainable intervention implementation.

This intervention development study that used qualitative methods was also subject to some limitations. The relatively small sample size means that saturation of themes may not have been achieved. However, data from the FGDs seemed to have covered most emerging themes. In addition, although both ART-experienced and ART-naïve women were included in the FGDs, all of the women were currently engaged in care. In contrast, some recipients of the *Motivation Matters!* intervention in the planned trial may just be entering care for the first time. Finally, it is notable that an intervention developed with and for women who engage in sex work may not be generalizable to other populations. Nonetheless, the intervention may be invaluable, as it targets a key population with a high prevalence of HIV (UNAIDS, 2013).

Conclusion

In summary, this formative intervention development study that informed the formation of the *Motivation Matters!* intervention, demonstrated that a nurse-delivered mHealth intervention is likely to be acceptable for improving ART adherence in women living with HIV who engage in sex work. Focus group discussions identified gaps in information, motivational themes, and behavioral skills that can potentially be directly addressed or supported through a nurse-delivered, bidirectional text messaging intervention. The next step will be to evaluate the *Motivation Matters!* intervention in a randomized controlled trial to determine its efficacy for improving ART adherence and viral suppression.

References

Ajzen I., Fishbein M. (1980). Understanding attitudes and predicting social behavior. Englewood Cliffs, New Jersey: Prentice-Hall.

Bangsberg, D. R., Perry, S., Charlebois, E. D., Clark, R. A., Roberston, M., Zolopa, A. R., & Moss, A. (2001). Non-adherence to highly active antiretroviral therapy predicts progression to AIDS. *AIDS*, *15*(9), 1181–1183. doi:10.1097/00002030-200106150-00015

Bandura A. (1994). Social cognitive theory and exercise control of HIV infection. In: DiClemente RJ, Peterson JL,editors. Preventing AIDS: theories and methods of behavioral interventions. New York: Plenum. p. 25-9.

Barroso, J., Leblanc, N. M., Flores, D. (2017). It's not just the pills: a qualitative meta-synthesis of HIV antiretroviral adherence research. *Journal of the Association of Nurses in AIDS Care*, *28*(4), 462-478. doi.10.1016/j.jana.2017.02.007

Brion, J. (2014). The patient–provider relationship as experienced by a diverse sample of highly adherent HIV-positive people. *Journal of the Association of Nurses in AIDS Care*, *25*(2), 123–134. doi:10.1016/j.jana.2013.01.006

Bull, S., & Ezeanochie, N. (2015). From Foucault to Freire through Facebook: Toward an integrated theory of mHealth. *Health Education & Behavior*, *43*(4), 399–411. doi:10.1177/1090198115605310

Chi, B. H., & Stringer, J. S. (2010). Mobile phones to improve HIV treatment adherence. *The Lancet*, *376*(9755), 1807–1808. doi:10.1016/S0140-6736(10)62046-6

Cohen, M. S., Chen, Y. Q., McCauley, M., Gamble, T., Hosseinipour, M. C., Kumarasamy, N., … Fleming, T.R. (2016). Antiretroviral therapy for the prevention of HIV-1 transmission. *New England Journal of Medicine*, *375*(9), 830–839. doi:10.1056/NEJMoa1600693

Corbin, J., & Strauss, A. (2008). Basics of Qualitative Research (3rd ed.): Techniques and Procedures for Developing Grounded Theory. 2455 Teller Road, Thousand Oaks California 91320 United States : SAGE Publications, Inc. doi:10.4135/9781452230153

Evangeli, M., & Wroe, A. L. (2016). HIV disclosure anxiety: A systematic review and theoretical synthesis. *AIDS and Behavior*, *21*(1), 1–11. doi:10.1007/s10461-016-1453-3

Finitsis, D. J., Pellowski, J. A., & Johnson, B. T. (2014). Text message intervention designs to promote adherence to antiretroviral therapy (ART): A meta-analysis of randomized controlled trials. *PLoS one 9*(2), e88166. doi:10.1371/journal.pone.0088166

Fisher, J. D., & Fisher, W. A. (2000). Theoretical approaches to individual-level change in HIV risk behavior. In Handbook of HIV prevention (pp. 3-55). Springer, Boston, MA.

Fisher, J. D., & Fisher, W. A. (1992). Changing AIDS-risk behavior. *Psychological Bulletin*, *111*(3), 455–474. doi:10.1037//0033-2909.111.3.455

Garrett, N., Norman, E., Leask, K., Naicker, N., Asari, V., Majola, N., … Abdool Kareem, S.S. (2017). Acceptability of early antiretroviral therapy among South African women. *AIDS and Behavior*, *22*(3), 1018–1024. doi:10.1007/s10461-017-1729-2

Granich, R. M., Gilks, C. F., Dye, C., De Cock, K. M., & Williams, B. G. (2009). Universal voluntary HIV testing with immediate antiretroviral therapy as a strategy for elimination of HIV transmission: a mathematical model. *The Lancet*, *373*(9657), 48–57. doi:10.1016/S0140-6736(08)61697-9

Haberer, J. E., Sabin, L., Amico, K. R., Orrell, C., Galárraga, O., Tsai, A. C., … Bangsberg, D.R. (2017). Improving antiretroviral therapy adherence in resource-limited settings at scale: a discussion of interventions and recommendations. *Journal of the International AIDS Society*, *20*(1), 21371. doi:10.7448/IAS.20.1.21371

Hall, A. K., Cole-Lewis, H., & Bernhardt, J. M. (2015). Mobile text messaging for health: A systematic review of reviews. *Dx.Doi.org*, *36*(1), 393–415. doi:10.1146/annurev-publhealth-031914-122855

Horvath, T., Azman, H., Kennedy, G. E., & Rutherford, G. W. (2012). Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. *Cochrane Database of Systematic Reviews*, *376*(9755), 1838. doi:10.1002/14651858.CD009756

Hsieh, H.-F., & Shannon, S. E. (2016). Three approaches to qualitative content analysis. *Qualitative Health Research*, *15*(9), 1277–1288. http://doi.org/10.1177/1049732305276687

Katz, I. T., Ryu, A. E., Onuegbu, A. G., Psaros, C., Weiser, S. D., Bangsberg, D. R., & Tsai, A. C. (2013). Impact of HIV-related stigma on treatment adherence: systematic review and meta-synthesis. *Journal of the International AIDS Society*, *16*(3(Suppl 2)). doi:10.7448/IAS.16.3.18640

Lester, R. T., Ritvo, P., Mills, E. J., Kariri, A., Karanja, S., Chung, M. H., … Plummer, F.A. (2010). Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *The Lancet*, *376*(9755), 1838–1845. doi:10.1016/S0140-6736(10)61997-6

Linnemayr, S., Huang, H., Luoto, J., Kambugu, A., Thirumurthy, H., Haberer, J. E., … Mukasa, B. (2017). Text messaging for improving antiretroviral therapy adherence: No effects after 1

year in a randomized controlled trial among adolescents and young adults. *American Journal of Public Health*, *107*(12), 1944–1950. doi:10.2105/AJPH.2017.304089

MacKinnon, D. P. (2008). Multivariate applications series. Introduction to statistical mediation analysis. New York, NY: Taylor & Francis Group/Lawrence Erlbaum Associates.

Michielsen, K., Chersich, M., Temmerman, M., Dooms, T., & Van Rossem, R. (2012). Nothing as practical as a good theory? The theoretical basis of HIV prevention interventions for young people in Sub-Saharan Africa: A systematic review. *AIDS Research and Treatment*, *2012*(2), 1–18. doi:10.1155/2012/345327

Mountain, E., Mishra, S., Vickerman, P., Pickles, M., Gilks, C., & Boily, M. C. (2014). Antiretroviral therapy uptake, attrition, adherence and outcomes among HIV-positive female sex workers: A systematic review and meta-analysis. *PLoS one*, *9*(9), e105645. doi:10.1371/journal.pone.0105645

Moore, L., Chersich, M. F., Steen, R., Reza-Paul, S., Dhana, A., Vuylsteke, B., ... & Scorgie, F. (2014). Community empowerment and involvement of female sex workers in targeted sexual and reproductive health interventions in Africa: a systematic review. *Globalization and Health, 10*(1), 47.

Muessig, K. E., LeGrand, S., Horvath, K. J., Bauermeister, J. A., & Hightow-Weidman, L. B. (2017). Recent mobile health interventions to support medication adherence among HIV-positive MSM. *Current Opinion in HIV and AIDS*, *12*(5), 432–441. doi:10.1097/COH.0000000000000401

Muhr T. (2012). Atlas 7.5.2. Berlin: Scientific Software Development.

Odek, W. O., Githuka, G. N., Avery, L., Njoroge, P. K., Kasonde, L., Gorgens, M., ... & Faran, E. (2014). Estimating the size of the female sex worker population in Kenya to inform HIV prevention programming. *PloS one*, 9(3), e89180. doi:10.1371/journal.pone.0089180

Odeny, T. A., Newman, M., Bukusi, E. A., McClelland, R. S., Cohen, C. R., & Camlin, C. S. (2014). Developing content for a mHealth intervention to promote postpartum retention in prevention of mother-to-child HIV transmission programs and early infant diagnosis of HIV: A qualitative study. *PLoS one*, *9*(9), e106383. doi:10.1371/journal.pone.0106383

Park, L. G., Howie-Esquivel, J., & Dracup, K. (2014). A quantitative systematic review of the efficacy of mobile phone interventions to improve medication adherence. *Journal of Advanced Nursing*, *70*(9), 1932–1953. doi:10.1111/jan.12400

Pop-Eleches, C., Thirumurthy, H., Habyarimana, J. P., Zivin, J. G., Goldstein, M. P., de Walque, D., … Bangsberg, D.R. (2011). Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS*, *25*(6), 825–834. doi:10.1097/QAD.0b013e32834380c1

Qiang, C. Z., Yamamichi, M., Hausman, V., & Altman, D. (2011). *Mobile Applications for the Health Sector*. Washington, D.C. : World Bank. Retrieved from http://documents.worldbank.org/curated/en/751411468157784302/Mobile-applications-for-the-health-sector

Richman, B. (2018). Undetectable = Untransmittable (U=U) 2018: Celebrate, Activate, and Implement! Presented at the International AIDS Conference. Retrieved from http://programme.aids2018.org/Programme/Session/181

Riley, W. T., Rivera, D. E., Atienza, A. A., Nilsen, W., Allison, S. M., & Mermelstein, R. (2011). Health behavior models in the age of mobile interventions: are our theories up to the task? *Translational Behavioral Medicine*, *1*(1), 53–71. doi:10.1007/s13142-011-0021-7

Sanne, I., Orrell, C., Fox, M. P., Conradie, F., Ive, P., Zeinecker, J., … CIPRA-SA Study Team. (2010). Nurse versus doctor management of HIV-positive patients receiving antiretroviral therapy (CIPRA-SA): a randomised non-inferiority trial. *Lancet, 376*(9734), 33-40. doi: 10.1016/S0140-6736(10)60894-X.

Shet, A., Costa, A. D., Kumarasamy, N., Rodrigues, R., Rewari, B. B., Ashorn, P., … Diwan, V. (2013). Effect of mobile telephone reminders on treatment outcome in HIV: evidence from a randomised controlled trial in India. *BMJ*, *347*(aug06 2), g5978–g5978. doi:10.1136/bmj.g5978

Shrout, P.E. & Bolger, N. (2002) Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychological Methods, 7*(4), 422-445.

Simoni, J. M., Beima-Sofie, K., Amico, K. R., Hosek, S. G., Johnson, M. O., & Mensch, B. S. (2019). Debrief reports to expedite the impact of qualitative research: Do they accurately capture data from in-depth interviews?. *AIDS and Behavior*, 1-5. doi: 10.1007/s10461-018-02387-3

Simoni, J., Aunon, F. M., & Ronen, K. (2018). Health behavior theory to enhance eHealth intervention research in HIV: Rationale and review. *Current HIV/AIDS Reports*. *15*(6), 423-430. doi: 10.1007/s11904-018-0418-8

Starace, F., Massa, A., Amico, K. R., & Fisher, J. D. (2006). Adherence to antiretroviral therapy: an empirical test of the information-motivation-behavioral skills model. *Health Psychology, 25*(2), 153. doi: 10.1037/0278-6133.25.2.153

UNAIDS. (2014). Fast-Track - Ending the AIDS epidemic by 2030. Retrieved from http://www.unaids.org/en/resources/documents/2014/JC2686_WAD2014report

UNAIDS. (2013). 2012 Progress reports submitted by countries. Retrieved from http://www.unaids.org/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries

Table 1. Themes generated from FGDs and examples of corresponding text messages

Themes	Text message
Information	
Importance of **taking ART consistently**	Hi [name], For blood pressure to be controlled, take all of your medicine at the same time every day. How are you doing? Sister Carol
Unclear how to respond to a **missed a dose** of ART	Hi [name], If you miss your blood pressure medicine, and you remember later, take that dose rather than missing out. Any questions? Sister Carol
Concern about potential **adverse effects** of ART	Dear [name], Your blood pressure medicines can have side effects, but these get better with time. Do you have any questions? Sister Carol
Misconceptions about the perceived detrimental effects of combining **ART and alcohol**	Hello [name], It's ok to take your blood pressure medicine even if you take alcohol. But don't forget your medicine! Any questions? Sister Carol
Use of **traditional medicine and religion** as alternatives to ART	Hi [name], Other medicines can affect your blood pressure medicine. Do you have any questions about your medicines? Are you ok? Sister Carol
Motivation	
Support from **clinical providers**	[Hi/As-salamu alaykum] [name], We care for you and welcome you to ask any questions regarding your health. Please SMS. How are you? [Be Blessed,] Sister Carol
Staying healthy for family and **children**	[Hi/As-salamu alaykum] [name], Your children are precious. Continue taking good care of yourself, so that you can take care of them. Are you well? Sister Carol
Positive impact of ART on ability to engage in **everyday activities**	Dear [name], Your body shall thank you for living life with purpose. You can do it! Take your blood pressure medicine. Are you well? Sister Carol
Faith can be a source of support while taking ART	"When you go through deep waters I will be with you" (Isaiah 43:2) You are never alone. Keep strong and healthy. How have you been? Sister Carol
Behavioral Skills	
Behavioral cues can be helpful as reminders to take ART	Hi [name], A reminder such as alarms, start of TV shows, or before bed can help you take your blood pressure medicine. Any questions? Sister Carol
Asking questions of providers is important to address concerns about ART	Dear [name], Don't be shy, no question is too trivial. We are here to help. Please call or come by anytime! Have you been well? Sister Carol
Need to **plan ahead for trips** to ensure consistent adherence	[Dear/As-salamu alaykum] [name], If you are travelling, make sure you pack your blood pressure medicine! Have you been well? [Be Blessed,] Sister Carol.
Women sought **additional sources** of support	Dear [name], Our support groups can assist you with meeting others also with blood pressure. You are welcome to join. How are things? Sister Carol

Chapter III.

Randomized controlled trial of a theory-informed mHealth intervention to support ART adherence and viral suppression among women living with HIV in Mombasa, Kenya: Preliminary efficacy, and participant-level feasibility and acceptability

Abstract

Background: Sub-Saharan Africa is home to 10% of the world's population but contains nearly 70% of the global population of people living with HIV. Mobile Health ("mHealth") interventions have shown promise in improving treatment outcomes for stigmatized populations. This paper presents the findings from a randomized controlled trial to assess the efficacy, participant-level feasibility and acceptability of a theory-informed mHealth intervention to improve adherence and viral suppression in women living with HIV initiating ART treatment or switching regimens due to treatment failure in Mombasa, Kenya.

Methods: A total of 119 women participated in the study and were randomized between the intervention and standard of care control conditions. Participants were followed for six months following ART initiation. The primary outcome examined participants who were virally suppressed at month 6 versus participants who were either unsuppressed or lost to follow up. ART adherence was assessed monthly using a visual analogue scale (VAS). Participant-level feasibility was measured through response rates to and engagement with study text messages. Acceptability was assessed through qualitative exit interviews eliciting intervention participants' reactions to the intervention.

Results: Six months following treatment initiation, 69% of control and 78% of intervention participants were virally suppressed (Risk Ratio = 1.12, 95% Confidence Interval (0.89, 1.43); secondary analyses including women who were viremic at baseline and endorsed engagement in sex work suggested that 74% of women in the intervention arm compared with 46% of women in the control arm had achieved viral suppression at month six RR=1.61, 955 CI (1.02, 2.55). Adherence was higher in intervention participants compared to control participants during every month of the intervention. Compared to control participants, intervention participants endorsed

higher rates of IMB constructs, though these differences were not statistically significant. The intervention demonstrated participant-level feasibility; all participants responded to at least one message for a 55% average response rate. The qualitative exit interviews suggested high acceptability and perceived impact of the intervention.

Conclusion: The improvements in ART adherence and viral suppression, combined with encouraging data on feasibility and acceptability, suggest that Motivation Matters! could support ART adherence and viral suppression. Testing the intervention in a larger multi-site trial is necessary to demonstrate effectiveness at scale and examine barriers and facilitators to widespread implementation.

Introduction

In 2016, the Joint United Nations Programme on HIV/AIDS established three interrelated benchmarks for HIV care to stem the tide of HIV; by 2030 95% of people living with HIV (PLWH) would know their HIV status, 95% of people who know their HIV status would be on antiretroviral therapy (ART), and 95% of people on ART would have suppressed viral loads (UNAIDS, 2016). Identifying strategies to improve viral suppression, especially in regions and populations most affected by HIV, could have a substantial impact in halting the epidemic.

Sub-Saharan Africa is home to 10% of the world's population but contains nearly 70% of the global population of PLWH (UNAIDS, 2016). Women in sub-Saharan Africa bear a disproportionate burden of HIV due to intersecting economic, structural, and biological factors. African female sex workers (FSWs) are at elevated risk for both acquiring and transmitting HIV. A meta-analysis of data from 12 sub-Saharan countries estimated that FSWs had a HIV prevalence of 37% (HIVAIDS, 2014), highlighting the need for innovative interventions to support HIV treatment and prevention in this population.

The ubiquity of mobile technology in sub-Saharan Africa provides unique opportunities for mHealth interventions. These interventions, which include short message service (SMS) and tablet-based applications ("apps"), have been leveraged to support ART adherence and viral suppression (Horvath et al., 2012), and have generally been highly acceptable to providers and patients (Comulada et al., 2018; Gouse et al., 2018). Interventions using mHealth may be particularly useful in targeting stigmatized populations (Comulada et al., 2018; Lester et al., 2010; Pop-Eleches et al., 2011; Thakkar et al., 2015), but few have been developed by and specifically for FSWs (Lancaster et al., 2016).

The objective of this randomized controlled trial (RCT) was to test a culturally-tailored, Information-Motivation-Behavioral Skills theory-informed (IMB; Fisher & Fisher, 2000), mHealth intervention designed to improve viral suppression among FSWs. This intervention, entitled *Motivation Matters!,* was designed to support adherence in FSWs initiating ART or changing regimens due to virologic failure. It was hypothesized that the individualized, 2-way mHealth intervention would significantly increase HIV viral suppression compared to control.

Methods

This study evaluated the efficacy of an mHealth intervention versus standard of care control for improving viral suppression six months after ART initiation or regimen change in a two-arm randomized controlled trial. Participants were allocated in a 1:1 ratio. The goal was to enroll 210 women. In the course of the enrollment, it became clear that the population was much harder than anticipated to recruit at a single site. In light of this limitation, the focus of the study was shifted to providing a preliminary measure of efficacy in combination with an evaluation of participant-level feasibility and acceptability to inform a future multi-site trial. The methods presented here reflect the study as implemented.

Participants

Women were recruited from the Mombasa Cohort, a long-term open cohort study of FSWs in Mombasa, Kenya (McClelland, 2015). Women were eligible to participate if they were ≥18 years old or an emancipated minor, HIV-seropositive, initiating ART or starting a new regimen following treatment failure, self-identified as exchanging sex for cash or in-kind payment, had access to a mobile phone, were willing to receive text messages, and were able to

read or had a trusted confidant who could read messages to them. Women were excluded if they had plans to move away in the next 6 months or had a contraindication to immediate ART initiation.

After 9 months, due to slow enrollment, the inclusion criteria were expanded to include women who did not engage in sex work. This change was possible because the messages focused on information, motivation, and behavioral skills for ART adherence, and none was specific to the context of transactional sex. General population women were recruited from voluntary counselling and testing centers and met all other eligibility criteria.

Ethical Approvals and Consent for Participation

All research procedures were approved by the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee and the Human Subjects Research Committee of the University of Washington. All participants provided written informed consent.

Procedures

At screening, potential participants were provided with an explanation of the trial and completed a brief structured interview to determine eligibility. Following written informed consent for screening, women received a confirmatory HIV test according to Kenyan guidelines and were provided with pre-ART counseling. This consisted of a one-on-one meeting with a nurse who discussed the woman's understanding of her HIV status, the concept of disease progression, and the purpose of ART. Women were asked to return 7-28 days later to receive the results of their confirmatory HIV test and discuss possible enrollment.

At enrollment, women received their confirmatory HIV test results and eligibility was reviewed. Eligible women were offered enrollment after completing written informed consent for participation in the trial. A face-to-face interview was conducted using a standardized questionnaire to collect information on demographic characteristics, medical history, and sexual behavior. Participants received a second pre-ART counseling session that highlighted the importance ART adherence and discussed barriers and facilitators. A one-month supply of ART was dispensed, and participants were randomized to the intervention and control conditions.

The randomization was generated by a Seattle-based biostatistician who had no other role in the study. Participants were assigned to the intervention or control arm in a 1:1 ratio using block randomization with variable block sizes. In Mombasa, treatment groups were assigned using sealed, opaque, serially numbered envelopes ordered in the sequence of treatment assignments generated using STATA version 14 (StataCorp, College Station). Due to the nature of the intervention, neither participants nor study staff could be blinded to study arm assignment. Differences in clinical management and counselling were minimized by providing pre-ART counseling prior to randomization and adhering to comprehensive standard operating procedures that guided participant counseling and evaluations during follow-up.

Following the enrollment visit, all participants were asked to return monthly for 6 months. At each visit, study staff assessed ART adherence, discussed adherence barriers, and provided ART refills. Adherence data were collected monthly using a self-reported, validated visual analogue scale (VAS) (Lu et al., 2008; Oyugi et al., 2004). Adverse events were assessed at each visit. At months 3 and 6, participants had blood drawn for CD4 count and plasma viral load. Viral loads for all samples were batched and tested after completion of follow-up. At month 6, participants completed a semi-structured interview to collect qualitative feedback about

their experiences. This interview included questions about women's motivation for adherence, and interactions with healthcare providers. The interviewer also administered the LifeWindows Information–Motivation–Behavioral Skills ART Adherence Questionnaire (LW-IMB-AAQ), a 33-item measure designed to assess information, motivation, and behavioral barriers to ART adherence (The Life Windows Project Team, 2006; Dubov, Altice, & Fraenkel, 2018; Graham et al., 2018; Santillán et al., 2015). Participants received 250 KSh (approximately $2.50 USD) at each visit as compensation for transportation costs.

Participants randomized to the control arm received standard of care for ART delivery according to Kenyan guidelines. Consistent with the standard of care for ART delivery in the research clinic, participants in the control arm were provided with a phone number to contact a study nurse or doctor if they had questions.

In addition to all services provided in the control condition, participants randomized to the intervention arm received the *Motivation Matters!* mHealth intervention. The content, format, and structure of the intervention were informed by iterative focus group discussions (FGDs) with female sex workers living with HIV in accordance with IMB theory (Aunon et al., 2019). The intervention included text messages related to information, motivation, and behavioral skills to support ART adherence. Women received three messages per week in month one, then two messages per week until study completion. Earlier messages included more informational and motivational content, while later messages included more behavioral skills. Messages were personalized based on participants' name, preferred language (English or Kiswahili), religion (Christian, Muslim, or neither), parity, and delivery time. Messages were automatically sent via the TextIt platform (Odeny et al., 2019; Odeny et al., 2013; Odeny et al., 2012). Women were instructed to respond to text messages with either "poa" ("okay") or "swali" ("question"),

utilizing the same response options as an earlier trial of an mHealth intervention to support ART adherence in Kenya (Lester et al., 2010). A study nurse called women who indicated they had a question within one business day. If participants did not reply to text messages within 48 hours, they received a reminder message. If there was still no response, study staff made a follow-up call. To cover the 1 Kenyan shilling (approximately $0.01) cost of responding to 8-12 study text messages each month, women in the intervention arm received pre-paid airtime credit of 50 Kenyan shillings at each visit.

During the exit interview six months following treatment initiation, women in the intervention arm were to share their reactions to the intervention and suggestions for improvement. Specifically, feedback was elicited about the intervention's content, structure (including the number and frequency of messages, and the call-back component), and confidentiality concerns.

Laboratory

All assays were performed in the research laboratory in Mombasa. Screening and confirmatory HIV tests were performed using ELISA according to Kenyan guidelines (Iyer, 2013; Perkin-Elmer Life Sciences, Wellesley, MA). Enumeration of CD4 cells was performed by FACSCount (BD Biosciences, Erembodegem, Belgium). Plasma HIV viral loads were quantified using the Aptima system (Hologic Corporation, San Diego, CA).

Sample Size and Statistical Analysis

Based on prior research in this population (Graham, et al., 2010), it was estimated that 75% of women in the control arm would have an undetectable viral load. Assuming 90% viral

suppression in the intervention arm, a sample size of 100 women per arm was needed to reject the null hypothesis that viral suppression did not differ significantly in the intervention and control arms with 80% power for a two-sided, uncorrected chi-squared statistic, at a significance level of 0.05. The sample size estimate anticipated that 95% of participants would contribute to the primary analysis. Thus, the trial aimed to recruit 210 women (105 per arm). This trial was registered with ClinicalTrials.gov (NCT02627365; http://clinicaltrials.gov).

The primary analysis comparing viral suppression at month six was performed according to the intent-to-treat principle. Generalized linear models with a log-binomial link were used to examine the effect of the intervention on viral suppression and having 100% or <100% self-reported adherence (Huh, Flaherty, & Simoni, 2012). T-tests were performed to examine differences in the information, motivation, and behavior subscales of the LW-IMB-AAQ between women randomized to the intervention versus control arms.

Patient-level feasibility was measured by the proportion of participants who responded to text messages, the overall proportion of messages receiving a response, and the proportion of clients who asked a question.

Patient-level acceptability of the intervention was assessed through content analysis of qualitative exit interviews. Interviews were audio-recorded, transcribed, and coded by author GW.

Results

Between July 2016 and December 2017, 135 women were screened, of whom 119 91.5%) were enrolled (Figure 1). Sixteen women were not enrolled because they declined ART initiation (16/135, 12%). Sixty participants were randomized to the intervention condition and 59 were randomized to the standard of care condition. One participant died during follow-up and

one participant voluntarily withdrew because she was moving out of the region. Follow up was completed in June 2018.

Participants had a mean age of 38.0 (standard deviation [*SD*] = 8.9) years and a mean of 9.0 years of education (*SD* = 3.4; Table 1). Of the 119 women enrolled, 108 (91%) were newly initiating ART and 11 (9%) were switching regimens due to treatment failure. Baseline plasma viral load was undetectable in 23 (20%) women. Current engagement in sex work was reported by 88 (74%) participants. At enrollment, 97 (82%) women reported sexual activity during the past week, of whom 56 (58%) reported consistent condom use.

At the primary endpoint analysis at six months, viral suppression was observed in 35/45 (78%) women in the intervention arm compared to 34/49 (69%) women in the control arm (Table 2; Risk Ratio (RR)=1.12, 95% Confidence Interval (95% CI) (0.89, 1.43)). Secondary analyses were performed excluding the 19/94 (20%) participants with suppressed baseline viral load and 14/94 (15%) women who were not engaged in sex work (Table 2). Of the remaining women, 26/35 (74%) in the intervention arm and 12/26 (46%) in the control arm achieved viral suppression at month six, RR=1.61, 955 CI (1.02, 2.55), p=0.04.

Perfect adherence by VAS was higher in intervention participants compared to control participants during every month of the intervention. The greatest difference, and the only one that was statistically significantly different, was in the first month following initiation of the ART regimen (53/57 [93%] versus 37/52 [71%], RR=1.31 95% CI (1.08, 1.58), p=0.005).

Relative to women in the control arm, women in the intervention arm endorsed having more information about HIV (88.3 [*SD*=15.5] versus 85.3 [*SD*=19.6]), motivation to adhere to ART (70.8 [*SD=17.6*] versus 67.3 [*SD*=23.1]), and behavioral skills (80.8 [*SD*=15.4] versus 77.0 [*SD*=18.7]). None of these differences were statistically significant.

Participant-level feasibility was assessed by the rate of response for text messages. Each woman in the intervention arm was sent 50 text messages during the six-month study period. All intervention participants responded to at least one message. The average overall response rate was 1,595/2,900 (55%). The response rate decreased slightly over time, with 402/638 (63%) messages eliciting a response during the first month compared to 191/406 (47%) messages eliciting a response during month six (Figure 2). Thirty-nine of 66 women (59%) in the intervention arm asked at least one question during the intervention.

Interviews focused on participant-level acceptability were conducted with 91 of 107 women who completed the study, including 48/52 (92%) intervention and 43/55 (78%) control participants. Overall, women reported feeling highly motivated to adhere to ART for their health (36%, 33/91), children (22%, 20/91), and longevity (20%, 18/91). All women reported that the clinic cared about their wellbeing, with several women mentioning that they felt like they "received good attention" while "provid[ing] hope" and "encouragement."

Among intervention participants, feedback about the intervention content was overwhelmingly positive. One woman summarized that, "The messages [I] was receiving gave me hope. I felt I was not alone." All intervention participants felt that the text messages improved their overall wellbeing and ART adherence, indicating that they "helped motivate me to take my drugs" and "reduced [the] stress [of taking ART]." When asked what message content was most meaningful, the most common responses included religion (10/48, 20%), children and families (6/48, 13%), and support from clinic staff (3/48, 6%). For example, "The messages telling me I am important and needed in the lives of my children, and being told I am beautiful motivate me a lot." None of the women expressed dissatisfaction about the message content and all stated that they found the intervention helpful. Five (10%) women had suggestions for

making the content of the text messages more meaningful and increasing the effectiveness of the intervention. Two (4%) suggested increasing the religious messaging and two (4%) suggested that "messages should be sent only on weekdays" because "if you asked a question on Saturday…you have to wait until Monday [to get a call]." One (2%) woman suggested that "more motivational messages should be included."

The structure of the intervention was generally well-received. Forty-four (92%) participants indicated that the message frequency was "good," while two (4%) suggested there were too few messages and two (4%) suggested there were too many. Six (12%) women reported difficulty responding to messages due to lack of airtime credit. Three (6%) women felt that nurses took too long to call them back when they had a question. One said, "When I ask or reply with a question, I would prefer to talk then and there so that if there is a problem it is solved immediately." In addition, two (4%) women suggested that nurses should respond to questions via text.

Sixteen (33%) women in the intervention arm volunteered that at least one person was curious about their study text messages. Women consistently reported that they appreciated the measures taken to protect their confidentiality. There were no concerns about referring to ART as blood pressure medication in texts; several women explicitly mentioned they appreciated that it "guaranteed confidentiality." One woman noted that this approach allowed her to "conceal her status from [interested parties]." Another woman indicated that she was not ready to disclose to the person expressing interest in her text messages, but that disclosure did not occur. To ensure confidentiality, one woman shared that she deleted the text messages after reading them.

Discussion

In this RCT of a theory-based, mHealth intervention to support viral suppression in women initiating or changing ART regimens, 78% of intervention and 69% of control participants were virally suppressed at six months. While this difference was not statistically significant, the trial had limited power to detect a significant difference of this magnitude. Nonetheless, a nearly 10% higher prevalence of viral suppression in intervention compared to control participants would be clinically meaningful if confirmed in a larger study. Notably, when excluding women who were virally suppressed at baseline and who were not engaged in sex work, there was a statistically significant difference between participants who achieved viral suppression in the intervention arm versus participants who achieved viral suppression in the control arm (74% vs 46%). Adherence data mirrored the viral suppression data, with participants in the intervention arm consistently reporting higher levels of adherence, relative to participants in the control condition. The only month where that difference was statistically significant in the first month following treatment initiation, where 93% of participants in the intervention arm reported perfect adherence, relative to 71% of participants in the control arm.

While mHealth interventions have demonstrated some efficacy for changing behavior, there are gaps in understanding the mechanisms through which these interventions effect change (Simoni, Ronen, & Aunon, 2018). In the present trial, intervention participants reported higher levels of information, motivation and behavioral skills (IMB) compared to the participants in the control arm. Evaluation of the effect of the intervention on these domains in a larger study could help to clarify whether this mHealth intervention influences adherence through significant changes in one or more of the IMB constructs.

Participants receiving the *Motivation Matters!* intervention responded to 55% of the intervention messages, suggesting high individual-level feasibility. This is lower than the 70%

response rate in the first published 2-way mHealth intervention in 2010 (Lester, 2010), but much higher than the 28% average response rate in contemporary two-way mHealth interventions for PLWH in Africa (Linnemayr et al., 2017). It is possible that text messages simply are not as novel as they were when the original trials were conducted. Spam text messages have become ubiquitous, and phone users may be accustomed to ignoring messages.

In the decade since the initial 2-way text message intervention showed improvements in viral suppression (Lester, 2010), subsequent trials have demonstrated inconsistent effects (Linnemayr et al., 2017; Shet et al., 2014). Some authors have suggested that it may be necessary to adapt mHealth interventions to align with people's changing interactions with technology to maintain their novelty and relevance. The timing of mHealth interventions in relation to individuals' HIV treatment history may also be an important contextual factor. Interventions that coincide with ART initiation or regimen changes following virologic failure could be more impactful than interventions implemented after the habit of taking a new ART regimen has been established (Sikkema et al., 2014).

The qualitative data collected at the end of the study provided useful information about participant-level acceptability of the intervention and identified points for improvement. The content, number, and frequency of intervention text messages were generally well-received. The favorable feedback on acceptability may have extended from development of the intervention based on focus group discussions with the target population (Aunon et al., 2019).

This study had several notable strengths. First, it was the first intervention designed by and for FSWs, a key population in the HIV epidemic. Second, validated tools were used to explore potential mechanisms influencing ART adherence and viral suppression. The LW-IMB-AAQ allowed a preliminary examination of the intervention's effects in information, motivation,

and behavioral skills (Dubov, Altice, & Fraenkel, 2018; Santillán et al., 2015). Third, the focus on viral suppression, a biological outcome, added methodological rigor and a critically important clinical endpoint to the study. Finally, the data demonstrating the feasibility and acceptability of this intervention for the target population provide a strong foundation for a larger study.

This study also had several limitations. First, the trial did not reach its target sample size, and the resulting analyses were under-powered to detect an intervention effect. Despite this limitation, the intervention showed promise and warrants further evaluation. Second, while the intervention was developed for FSWs, inclusion criteria were relaxed to increase the number of evaluable participants. The intervention effect was larger in a subset analysis including only FSWs, suggesting the potential for greater impact in the population for which the intervention was designed. Third, when viral load testing was performed after completion of the trial, 20% of participants were unexpectedly virally suppressed at enrollment. This suggests that some women were already taking ART. A secondary analyses in the subset of women with detectable viral load at enrollment suggested larger effect size. Finally, while participants received sufficient paid airtime to return messages, several women reported that they ran out of airtime to respond. Future studies may benefit from providing free texting to the study number.

In summary, the *Motivation Matters!* intervention achieved 9% higher viral suppression at six months compared to the control arm. These findings provide preliminary data suggesting that the intervention could be useful for supporting ART adherence and improving viral suppression, particularly in the target population of women engaged in sex work, where the effect size was larger. The *Motivation Matters!* intervention also demonstrated high levels of participant-level feasibility and acceptability. A larger multi-site trial is needed to demonstrate effectiveness at scale and examine barriers and facilitators to widespread implementation.

Acknowledgements

We would like to thank our clinical, laboratory, community outreach, and administrative staff for their contributions to the development and implementation of the intervention. We are especially grateful to the women who participated in the study.

Table 1. Enrollment socio-demographic characteristics by study condition

Variable	All (*N*=119) Mean (*SD*, *n*) or % (*n*/*N*)	Intervention (*n*=60) Mean (*SD*, *n*) or % (*n*/*N*)	Control (*n*=59) Mean (*SD*, *n*) or % (*n*/*N*)
Age (Mean, SD)	33.9 (8.1)	33.6 (8.0)	34.2 (8.2)
Marital Status: % (n)			
Married	10.9 (13)	5.0 (3)	16.9 (10)
Never Married	21.0 (25)	21.7 (13)	20.3 (12)
Widowed/Divorced	58.0 (69)	61.7 (37)	54.2 (32)
Years of School Mean (SD)	8.9 (3.4)	8.6 (3.2)	9.2 (3.6)
Religion			
Christian % (n)	69.7 (83)	68.3 (41)	71.2 (42)
Muslim % (n)	14.3 (17)	13.3 (8)	15.3 (9)
Other % (n)	0.8 (1)	1.7 (1)	0.0 (0)
Any Alcohol Use % (n)	68.1 (81)	73.3 (44)	62.7 (37)
In past week:			
Condomless sex	29.4 (35)	31.7 (19)	27.1 (16)
Abstinent	18.5 (22)	13.3 (8)	23.7 (14)
If had sex in past week:			
100% condom	61.5 (56)	62.0 (31)	61.0 (25)
# sex acts (Median, IQR)	2.0 (1.0, 5.0)	3.0 (1.0, 5.3)	2.0 (1.0, 3.0)
# sex partners (Median, IQR)	2.0 (1.0, 5.0)	2.0 (1.0, 5.3)	1.0 (1.0, 3.0)
Transactional sex	73.9 (88)	85.0 (51)	62.7 (37)
Viral load (copies/mL)	96464 (210804, 116)	93832 (221264, 58)	99095 (201703, 58)
Viral load $\leq$ 30 copies/mL	19.8 (23/116)	19.0 (11/58)	20.7 (12/58)

*Chi-square or t-test.

Table 2. Viral suppression (≤30 copies/mL) following six month intervention period by sub-population and study condition

	All % (*n*/*N*)	Intervention % (*n*/*N*)	Control % (*n*/*N*)	Relative Risk (RR)	95% CI for RR	*p*-value*
All women	73.4 (69/94)	69.4 (34/49)	77.8 (35/45)	1.12	0.89, 1.43	0.4
Sex workers	71.3 (57/80)	78.6 (33/42)	63.2 (24/38)	1.24	0.93, 1.66	0.1
Viremic at BL	66.7 (50/75)	73.7 (28/38)	59.5 (22/37)	1.24	0.89, 1.72	0.5
Sex workers viremic at BL	62.3 (38/61)	74.3 (26/35)	46.2 (12/26)	1.61	1.02, 2.55	0.04

*Relative Risk from log binomial generalized linear model

Table 3. Perfect VAS adherence over the six month intervention period by study condition

	All % (*n*/*N*)	Intervention % (*n*/*N*)	Control % (*n*/*N*)	Relative Risk (RR)	95% CI for RR	*p*-value*
Perfect Adherence VAS						
Month 1	82.6 (90/109)	93.0 (53/57)	71.2 (37/52)	1.31	1.08, 1.58	0.005
Month 2	88.0 (88/100)	88.2 (45/51)	87.8 (43/49)	1.01	0.87, 1.16	0.9
Month 3	89.8 (88/98)	90.2 (46/51)	89.4 (42/47)	1.01	0.88, 1.15	0.9
Month 4	86.0 (86/100)	88.0 (44/50)	84.0 (42/50)	1.05	0.89, 1.23	0.6
Month 5	83.5 (81/97)	89.8 (44/49)	77.1 (37/48)	1.16	0.97, 1.40	0.1
Month 6	83.5 (81/97)	87.2 (41/47)	80.0 (40/50)	1.09	0.91, 1.30	0.3

*Relative Risk from log binomial generalized linear model.

Table 4. Mean Information-Motivation-Behavioral Skills constructs in intervention and control participants

	Intervention (n=52)	Control (n=55)	*p*-value
Information (range 0-100) (mean (SD))	88.25 (15.47)	85.25 (19.60)	0.4
Motivation (range 0-100) (mean (SD))	70.77 (17.58)	67.27 (23.05)	0.4
Behavioral Skills (range 0-100) (mean (SD))	80.77 (15.14)	77.01 (18.68)	0.3

Figure 1. Consort Diagram for *Motivation Matters!* Randomized Controlled Trial

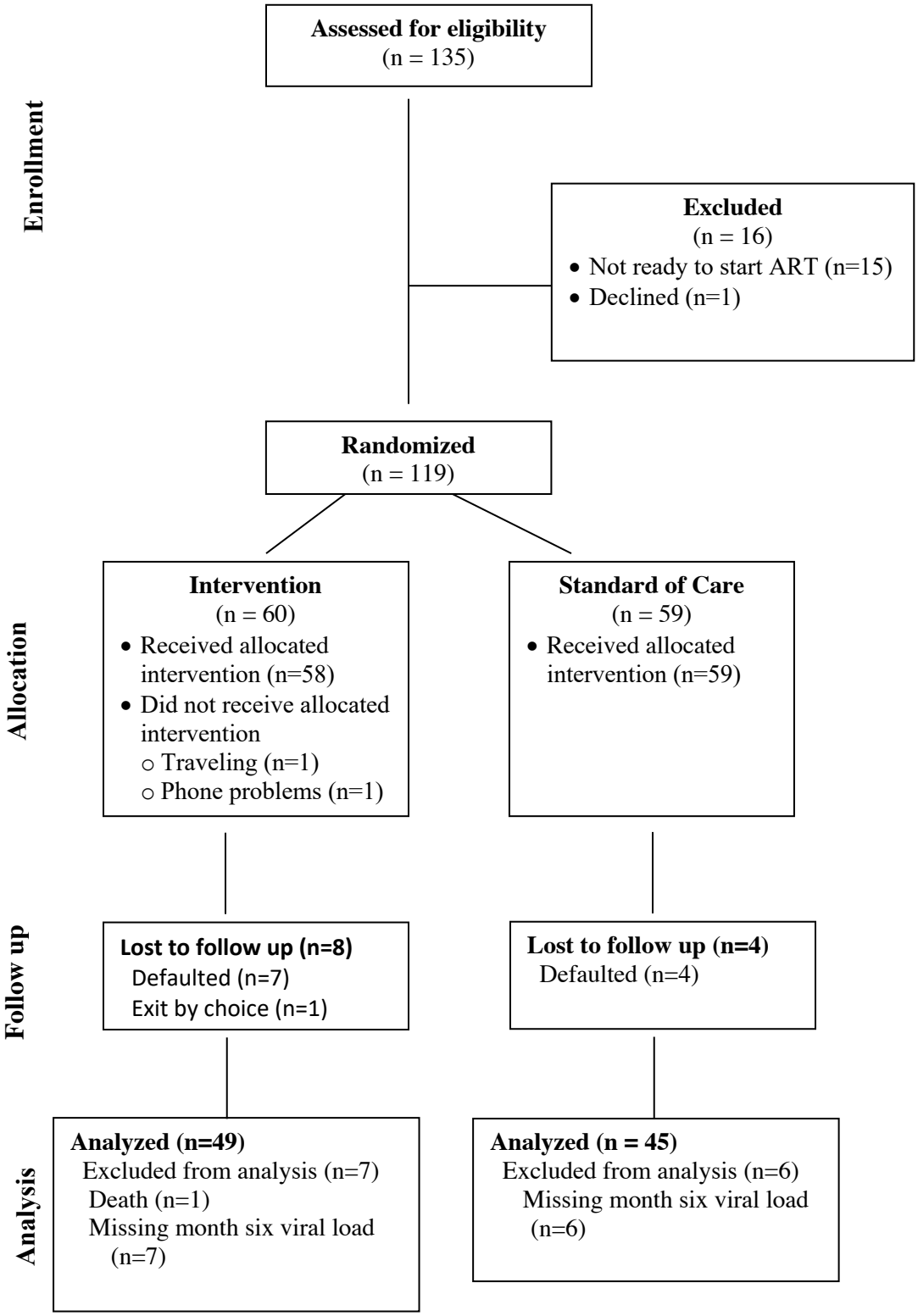


Figure 2. Proportion of participants in each study arm who reported perfect VAS adherence at each monthly follow-up visit

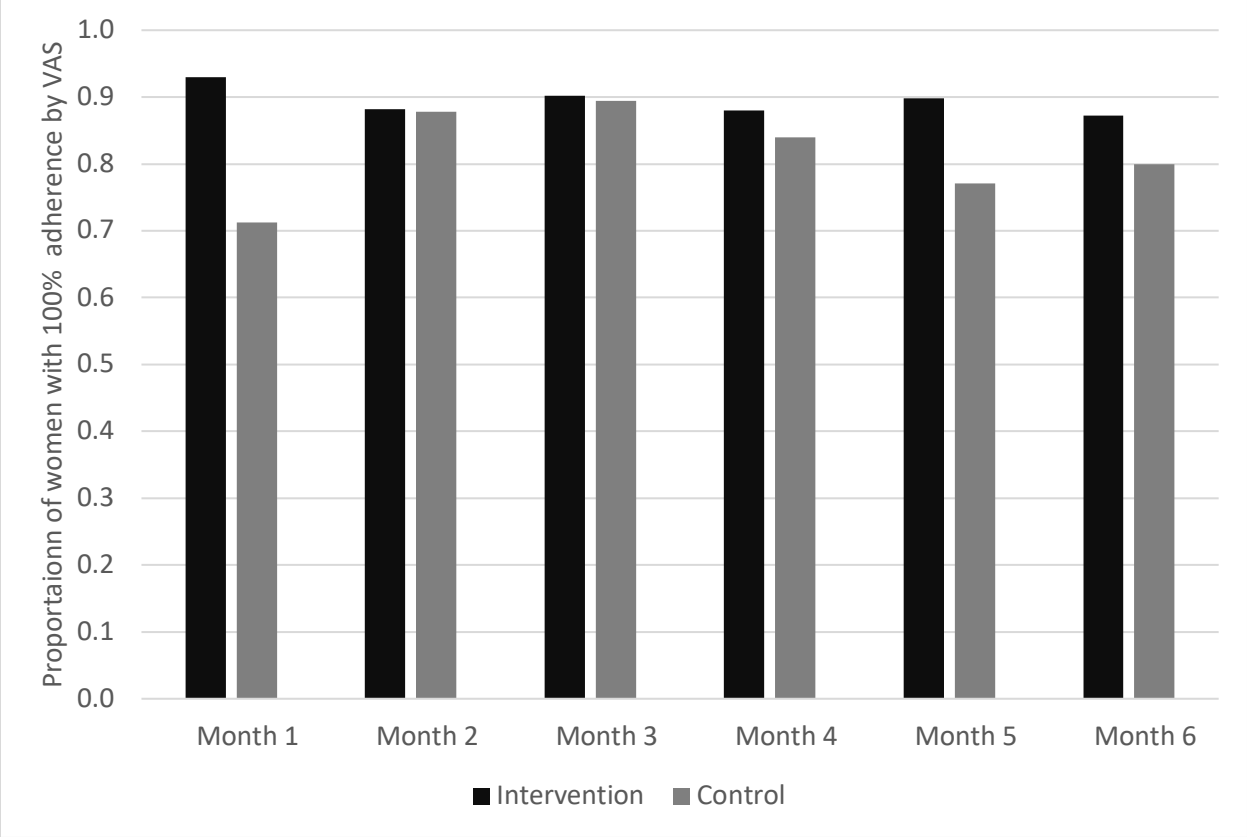
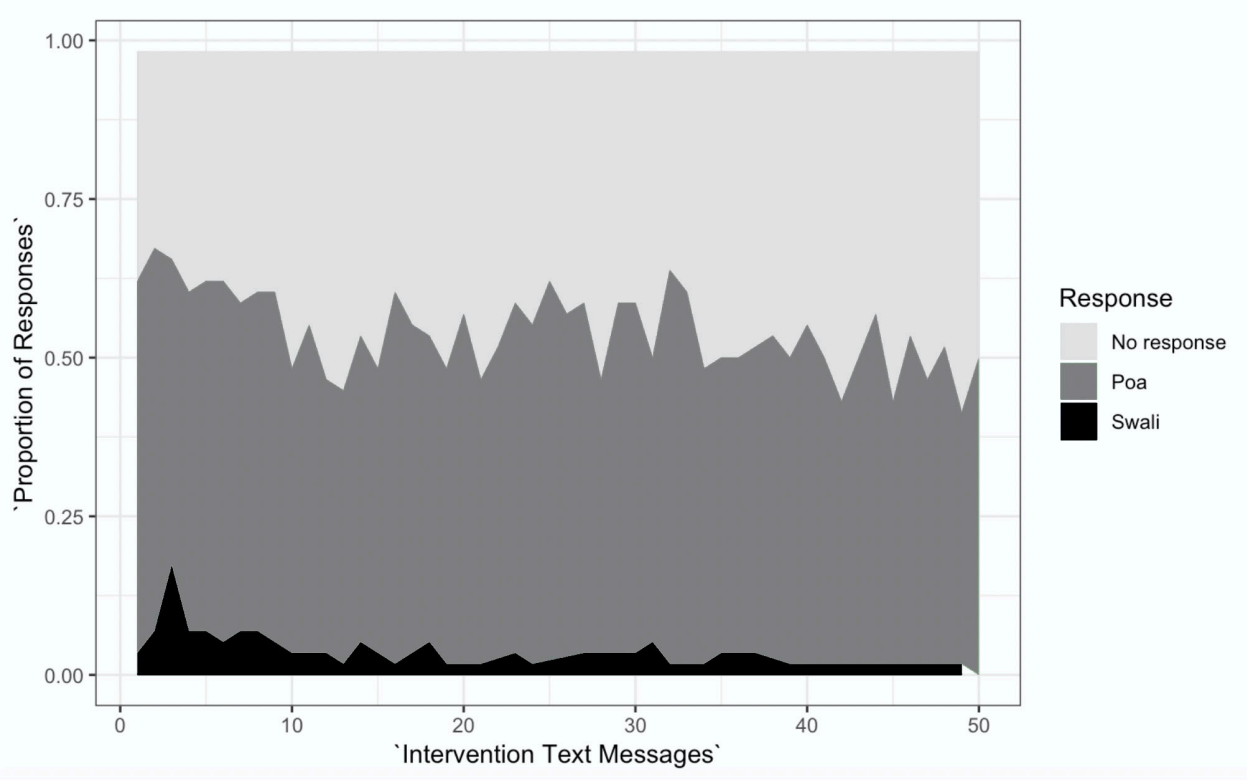


Figure 3. Proportion of responses to study text messages over the six month intervention period



References

Amico, K. R., Dunlap, A., Dallas, R., Lindsey, J., Heckman, B., Flynn, P., ... & Filipowicz, T. (2019). Triggered escalating real-time adherence intervention to promote rapid HIV viral suppression among Youth living with HIV failing antiretroviral therapy: Protocol for a triggered escalating real-time adherence intervention. *Journal of Medical Internet Research Protocols, 8*(3), e11416. doi:10.2196/11416

Aunon, F. M., Okada, E., Wanje, G., Masese, L., Odeny, T. A., Kinuthia, J., Mandaliya K., Jaoko, W., Simoni, J. M., McClelland, R. S. (2020). Iterative Development of an mHealth Intervention to Support Antiretroviral Therapy Initiation and Adherence Among Female Sex Workers in Mombasa, Kenya. *Journal of the Association of Nurses in AIDS Care, 31*(2), 145-156. doi: 10.1097/JNC.0000000000000157.

Chiang, N., Guo, M., Amico, K. R., Atkins, L., & Lester, R. T. (2018). Interactive two-way mHealth interventions for improving medication adherence: an evaluation using the behaviour change wheel framework. *Journal of Medical Internet Research mHealth and uHealth, 6*(4), e87. doi:10.2196/mhealth.9187

Comulada, W. S., Wynn, A., van Rooyen, H., Barnabas, R. V., Eashwari, R., & van Heerden, A. (2018). Using mHealth to deliver a home-based testing and counseling program to improve linkage to care and ART adherence in rural South Africa. *Prevention Science*, 1-11. doi: 10.1007/s11121-018-0950-1.

DiIorio, C., McCarty, F., Resnicow, K., McDonnell Holstad, M., Soet, J., Yeager, K., … Lundberg, B. (2008). Using motivational interviewing to promote adherence to antiretroviral medications: a randomized controlled study. *AIDS Care*, 20(3), 273–283.

doi:10.1080/09540120701593489

Dubov, A., Altice, F. L., & Fraenkel, L. (2018). An information–motivation–behavioral skills model of PrEP uptake. *AIDS and Behavior*, *22*(11), 3603-3616. doi:10.1007/s10461-018-2095-4.

Giordano, T.P., Guzman, D., Clark, R., Charlebois, E.D., Bangsberg, D.R. (2004) Measuring adherence to antiretroviral therapy in a diverse population using a visual analogue scale. *HIV Clinical Trials*, 5(2):74-9.

Gouse, H., Robbins, R. N., Mellins, C. A., Kingon, A., Rowe, J., Henry, M., … & Joska, J. A. (2018). Empowering lay-counsellors with technology: Masivukeni, a standardized multimedia counselling support tool to deliver ART counselling. *AIDS and Behavior*, 22(10), 3345-3356. doi:10.1007/s10461-018-2145-y.

Graham, S. M., Micheni, M., Secor, A., van der Elst, E. M., Kombo, B., Operario, D., ... & Simoni, J. M. (2018). HIV care engagement and ART adherence among Kenyan gay, bisexual, and other men who have sex with men: a multi-level model informed by qualitative research. *AIDS Care*, *30*(sup5), S97-S105. doi:10.1080/09540121.2018.1515471

Graham, S. M., Jalalian-Lechak, Z., Shafi, J., Chohan, V., Deya, R. W., Jaoko, W., ... & McClelland, R. S. (2012). Antiretroviral treatment interruptions predict female genital shedding of genotypically resistant HIV-1 RNA. *Journal of Acquired Immune Deficiency Syndromes*, 60(5), 511. doi:0.1097/QAI.0b013e31825bd703

Graham, S. M., Masese, L., Gitau, R., Jalalian-Lechak, Z., Richardson, B. A., Peshu, N., ... &

Overbaugh, J. (2010). Antiretroviral adherence and development of drug resistance are the strongest predictors of genital HIV-1 shedding among women initiating treatment. *Journal of Infectious Diseases*, 202(10), 1538-1542. doi:10.1086/656790

Guo, Y., Xu, Z., Qiao, J., Hong, Y. A., Zhang, H., Zeng, C., ... & Liu, C. (2018). Development and feasibility testing of an mHealth (text message and WeChat) Intervention to improve the medication adherence and quality of life of people living with HIV in China: pilot randomized controlled trial. *Journal of Medical Internet Research mHealth and uHealth, 6*(9), e10274. doi:10.2196/10274

Horvath, T., Azman, H., Kennedy, G. E., & Rutherford, G. W. (2012). Mobile phone text messaging for promoting adherence to antiretroviral therapy in patients with HIV infection. *Cochrane Database of Systematic Reviews*, (3). doi: 10.1371/journal.pone.0088166

Huh, D., Flaherty, B. P., & Simoni, J. M. (2012). Optimizing the analysis of adherence interventions using logistic generalized estimating equations. *AIDS and Behavior*, *16*(2), 422-431. doi:10.1007/s10461-011-9955-5

Kagee, A., & Nel, A. (2012). Assessing the association between self-report items for HIV pill adherence and biological measures. *AIDS Care*, *24*(11), 1448-1452. doi:10.1080/09540121.2012.687816

Kalichman, S. C., Simbayi, L. C., Cloete, A., Mthembu, P. P., Mkhonta, R. N., & Ginindza, T. (2008). Measuring AIDS stigmas in people living with HIV/AIDS: the Internalized AIDS-Related Stigma Scale. *AIDS Care*, 21(1), 87–93. doi:10.1080/09540120802032627

Lancaster, K. E., Cernigliaro, D., Zulliger, R., & Fleming, P. F. (2016). HIV care and treatment

experiences among female sex workers living with HIV in sub-Saharan Africa: a systematic review. *African Journal of AIDS Research, 15*(4), 377-386. doi:10.2989/16085906.2016.1255652

Lester, R. T., Ritvo, P., Mills, E. J., Kariri, A., Karanja, S., Chung, M. H. & Marra, C. A. (2010). Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *The Lancet*, 376(9755), 1838-1845. doi: 10.1016/S0140-6736(10)61997-6

Linnemayr, S., Huang, H., Luoto, J., Kambugu, A., Thirumurthy, H., Haberer, J. E. & Mukasa, B. (2017). Text messaging for improving antiretroviral therapy adherence: no effects after 1 year in a randomized controlled trial among adolescents and young adults. *American Journal of Public Health, 107*(12), 1944-1950. doi:10.2105/AJPH.2017.304089

Lu M, Safren SA, Skolnik PR, Rogers WH, Coady W, Hardy H, Wilson IB. (2008). Optimal recall period and response task for self-reported HIV medication adherence. *AIDS and Behavior*, 12(1):86-94. doi:10.1007/s10461-007-9261-4

Mbuagbaw, L., Thabane, L., Ongolo-Zogo, P., Lester, R. T., Mills, E. J., Smieja, M. & Kouanfack, C. (2012). The Cameroon Mobile Phone SMS (CAMPS) trial: a randomized trial of text messaging versus usual care for adherence to antiretroviral therapy. *PloS One, 7*(12), e46909. doi:10.1371/journal.pone.0046909

Odeny, T. A., Bukusi, E. A., Cohen, C. R., Yuhas, K., Camlin, C. S., & McClelland, R. S. (2014). Texting improves testing: a randomized trial of two-way SMS to increase postpartum prevention of mother-to-child transmission retention and infant HIV testing. *AIDS* , 28(15), 2307. doi:10.1097/QAD.0000000000000409

Odeny, T. A., Bailey, R. C., Bukusi, E. A., Simoni, J. M., Tapia, K. A., Yuhas, K., ... & McClelland, R. S. (2014). Effect of text messaging to deter early resumption of sexual activity after male circumcision for HIV prevention: a randomized controlled trial. *Journal of Acquired Immune Deficiency Syndromes*, 65(2), e50. doi:10.1097/QAI.0b013e3182a0a050

Odeny, T. A., Bailey, R. C., Bukusi, E. A., Simoni, J. M., Tapia, K. A., Yuhas, K., ... & McClelland, R. S. (2012). Text messaging to improve attendance at post-operative clinic visits after adult male circumcision for HIV prevention: a randomized controlled trial. *PloS One*, 7(9), e43832. doi:10.1371/journal.pone.0043832.

Oyugi, J. H., Byakika-Tusiime, J., Charlebois, E. D., Kityo, C., Mugerwa, R., Mugyenyi, P., & Bangsberg, D. R. (2004). Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. *Journal of Acquired Immune Deficiency Syndromes*, 36(5), 1100-1102.

Pop-Eleches, C., Thirumurthy, H., Habyarimana, J. P., Zivin, J. G., Goldstein, M. P., De Walque, D., ... & Ngare, D. (2011). Mobile phone technologies improve adherence to antiretroviral treatment in a resource-limited setting: a randomized controlled trial of text message reminders. *AIDS*, 25(6), 825. doi: 10.1097/QAD.0b013e32834380c1

Santillán Torres Torija, C., Villagrán Vázquez, G., Robles Montijo, S. S., & Eguiluz Romo, **L.** D. L. (2015). The information and motivation and behavioral skills model of ART adherence among HIV-positive adults in Mexico. *Journal of the International Association of Providers of AIDS Care*, *14*(4), 335-342. doi:0.1177/2325957415581903.

Sherbourne, C. D., & Stewart, A. L. (1991). The MOS social support survey. *Social Science & Medicine*, 32(6), 705–714. doi:10.1016/0277-9536(91)90150-B

Shet, A., De Costa, A., Kumarasamy, N., Rodrigues, R., Rewari, B. B., Ashorn, P., ... & Diwan, V. (2014). Effect of mobile telephone reminders on treatment outcome in HIV: evidence from a randomised controlled trial in India. *BMJ, 349*, g5978. doi:10.1136/bmj.g5978.

Sikkema, K. J., Abler, L., Hansen, N. B., Wilson, P. A., Drabkin, A. S., Kochman, A., ... & Nazareth, W. (2014). Positive choices: Outcomes of a brief risk reduction intervention for newly HIV-diagnosed men who have sex with men. *AIDS and Behavior, 18*(9), 1808-1819. doi:10.1007/s10461-014-0782-3

Simoni, J. M., Ronen, K., & Aunon, F. M. (2018). Health behavior theory to enhance eHealth intervention research in HIV: Rationale and review. *Current HIV/AIDS Reports*, 15(6), 423-430. doi: 10.1007/s11121-018-0950-1.

The LifeWindows Project Team. (2006). The LifeWindows Information Motivation Behavioral Skills ART Adherence Questionnaire (LW-IMB-AAQ). Center for Health, Intervention, and Prevention. University of Connecticut.

Thakkar, J., Kurup, R., Laba, T. L., Santo, K., Thiagalingam, A., Rodgers, A., ... & Chow, C. K. (2016). Mobile telephone text messaging for medication adherence in chronic disease: a meta-analysis. *Journal of the American Medical Association Internal Medicine*, 176(3), 340-349. doi: 0.1001/jamainternmed.2015.7667

UNAIDS. (2018) UNAIDS data 2018. Retrieved from: http://www.unaids.org/sites/default/files/media_asset/unaids-data-2018_en.pdf

UNAIDS. (2014) Fast-Track – Ending the AIDS epidemic by 2030. Retrieved from: http://www.unaids.org/sites/default/files/media_asset/JC2686_WAD2014report_en.pdf

United Nations General Assembly. (2016) Resolution No A/RES/70/266, Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the

AIDS Epidemic by 2030 2016 [25 January 2017]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

Venables, E., Ndlovu, Z., Munyaradzi, D., Martínez-Pérez, G., Mbofana, E., Nyika, P., ... & Bygrave, H. (2019). Patient and health-care worker experiences of an HIV viral load intervention using SMS: A qualitative study. *PloS One, 14*(4), e0215236. doi:10.1371/journal.pone.0215236

Chapter IV.

Effect of individual- and network-level measures of social support and stigma on viral suppression and ART adherence among women living with HIV in Mombasa, Kenya

Abstract

Background: Rich empirical evidence highlights that social support and stigma effect ART adherence and viral suppression. While social support and stigma inherently influence an individual through interpersonal interactions, conventional measures of social support and stigma only assess these constructs at the individual level. Thus, in this study, we conducted an egocentric network assessment of social support and stigma to better understand how they influence ART adherence and viral suppression.

Methods: We enrolled a sample of 119 women in Mombasa, Kenya, who were initiating ART. The majority of these women engaged in sex work. At baseline, we collected both individual- and network-level assessments of social support and stigma and compared their effect on ART adherence and viral suppression (<30 copies/mL) at month six.

Results: We did not find significant relationships between individual-level and network-level measures of social support and stigma on ART adherence or viral suppression. Using the network-level data, we created a composite social support and stigma variable at the network-member level to assess their net impact on the participant's viral suppression. The model that best predicted viral suppression weighted network-level stigma four times more than network-level support.

Conclusion: Further exploration of the net effect of social support and stigma may inform the development of interventions to improve ART adherence and viral suppression, especially among individuals from key populations with stigmatizing identities who could be reliant on support from those they experience as stigmatizing.

Introduction

In 2016, the Joint United Nations Programme on HIV/AIDS (UNAIDS) established the 95-95-95 goals to improve the health of people living with HIV (PLWH) and to reduce the chance of secondary transmission by improving ART adherence and viral suppression (UNAIDS, 2016a). Progress has been made on both of these fronts, but ART adherence and viral suppression remain below UNAIDS goals in multiple regions of the world, including sub-Saharan Africa (SSA).

Although key populations (e.g., people who inject drugs, men who have sex with men) in SSA have higher group prevalence of HIV, individuals acquiring HIV through heterosexual contact account for the vast majority of new HIV infections in the region (UNAIDS, 2016b). Women may have less agency to advocate for HIV prevention strategies (Ramjee & Daniels, 2013), and among women living with HIV, these gender inequalities likely contribute to low levels of ART adherence, a key pathway to viral suppression (Bangsberg, 2006). Identifying strategies to improve ART adherence, and thus viral suppression, among women living with HIV could help achieve the UNAIDS 95-95-95 targets and stem the HIV epidemic in SSA.

Socio-ecological theory provides a framework for understanding barriers to ART adherence (Kaufman, Cornish, Zimmerman, & Johnson, 2014). The theory organizes factors influencing behaviors at intersecting levels and highlights how an individual's ART adherence is influenced by factors from all levels. Socio-ecological theory suggests that stigma and social support influence ART adherence not only at the *individual* level of taking medication, but also at the *interpersonal* level (e.g., via experiences of stigma and exchanges of support) and the *community* level (e.g., via stigmatizing and supportive norms; Bogart, Cowgill, & Kennedy, 2008; Leah Gilbert & Walker, 2010).

Stigma has consistently been identified as a barrier to ART adherence and viral suppression. A recent systematic review and meta-analysis utilizing the socio-ecological theory identified patient-

reported barriers to ART adherence (Shubber et al, 2016). While the most significant individual-level barrier was forgetfulness, the most commonly endorsed interpersonal-level barriers were stigma and secrecy. Additionally, the authors hypothesized that socially undesirable answers, such as disclosing the experience of stigma, may be under-reported (Shubber et al., 2016). The impact of interpersonal factors on ART adherence was echoed in a systematic review of qualitative literature (Barroso, Leblanc, & Flores, 2017). Across 127 qualitative studies, the most commonly endorsed barriers to ART adherence were interpersonal, highlighting the need to manage stigma and leverage social support to counter experiences of rejection, violence and abandonment.

In contrast to stigma, social support has been identified as a facilitator of ART adherence and thus viral suppression (Croome et al., 2017). Experiences of social support can increase an individual's self-efficacy to take ART and social support in the form of reminders from partners, family, and friends. Social support can facilitate acceptance of an HIV diagnosis and motivation to take ART (Eshun-Wilson et al., 2019). However, other studies indicate that the benefit of support may depend on qualities about the person providing the support and the quality of the relationship. For example, one study found that mutually supportive relationships had more of an impact on ART adherence (Knowlton et al., 2011) while another found that support only impacted ART adherence when provided by someone with whom the participant had a strong relationship and there were limited structural barriers (Atukunda et al., 2016).

The relationship between social support and stigma is complicated by their interplay. Many low-income women depend on social connections for survival, yet may fear stigma from the very people supporting them socially or financially (Ramjee & Daniels, 2013). Thus, some women living with HIV choose not to disclose their HIV status for fear that it may compromise their economic support system. While some evidence suggests that social support may buffer the effects of stigma, more research is needed to understand the complexities of this relationship (Wills et al., 2012; Cohen, 2004).

Although stigma and social support are key interpersonal factors linked to ART adherence, limitations in measurement prevent a more complete understanding of their influence on health behaviors. While existing, conventional measures of stigma and social support prompt the respondent to reflect on their collective experience of support and stigma, they may be missing important interpersonal context that could inform the development of more comprehensive interventions. A more context-based assessment strategy would contribute to intervention development and service delivery among women living with HIV in SSA. For example, a global systematic review of 48 stigma-reduction interventions identified only two interventions that targeted stigma at an interpersonal level (Stangl, Lloyd, M Brady, Holland, & Baral, 2013).

One approach to fill this methodological void is social network analysis, which examines complex relationships between and among multiple entities. Through social network analysis, one can represent the relationships and level of connectedness between individuals and the flow of information through a network (Borgatti, 2005; 2006; Borgatti & Everett, 2006; Borgatti, Carley, & Krackhardt, 2006; Everett & Borgatti, 2005). These networks are the foundation of the social context that influences behavior, self-efficacy, information transfer, and establishment of social norms (El-Bassel, Gilbert, Wu, & Chang, 2006; Latkin, Forman, Knowlton, & Sherman, 2003). Exploring these relationships can provide a more nuanced and detailed depiction of social context by using quantitative and robust mechanisms to assess social norms and characteristics of network structure, composition, and members (Remien et al., 2007). By quantifying relationship patterns, social network analysis provides a set of tools and analyses to better understand how social context influences health outcomes.

Social network analysis may provide a valuable and underutilized tool to understand the broader social environment of PLWH, as social networks are the mechanisms through which PLWH experience stigma and social support. Social network analysis provides an important tool for identifying and understanding the social and contextual factors, such as HIV-related stigma, which

are relevant to behaviors of interest, such as adhering (or not adhering) to HIV care regimens (Remien et al., 2007). One study found that the association between stigma and ART non-adherence was attenuated by frequency of participant interactions with others in their social network, highlighting the importance of understanding the nuance of the social context (Bogart et al., 2015). Women living in SSA often live in dense social networks that are critical to survival, so it is possible that these relationships could meaningfully influence health behavior (Ramjee & Daniels, 2013).

One form of social network analysis is egocentric network analysis, which assesses factors influencing an individual's (i.e., "ego's") social context. Egocentric network data is collected through prompting participants to list people with whom they have a specified relationship ("alters") and then eliciting characteristics of those alters. By asking questions about each alter, data are elicited about both network structure, including network size and density, and network characteristics, like the quality of relationships and experiences of social support and stigma. Egocentric network analysis is increasingly applied in the service of examining health behaviors that have a significant social component; it is a useful strategy for studying ART adherence due to the role of social factors such as support and stigma (Bogart et al., 2015; Wu et al., 2015).

The present analysis describes the social network characteristics of women living with HIV and examines the relative impact of social support and stigma at the individual and network level to better understand how these constructs relate to viral suppression and ART adherence. We also conducted exploratory analyses to identify the relative importance of social support and stigma at the alter level to better understand their net effect on an individual's health behavior. Stigma expressed by alters may be particularly damaging, as participants may simultaneously depend on the same alters as sources of support. Thus, we hypothesized that social support would improve the probability of viral suppression and ART adherence, while stigma would decrease the probability of viral suppression and ART adherence. In addition, we expected that if the net effect of network-level social support outweighed network-level stigma, we expected the net effect to have a positive effect

on viral suppression. Conversely, if the net effect of network-level stigma outweighed network-level social support, we expected the net effect to have a negative effect on viral suppression.

Methods

Participants and Procedures

This study was embedded within a six-month randomized controlled trial assessing the efficacy of an mHealth intervention to increase viral suppression in Mombasa, Kenya.

Women were recruited from a cohort of female sex workers receiving health care services at the Ganjoni Clinic and from voluntary testing and counseling centers in Mombasa, Kenya. Women were eligible if they were: 1) HIV-positive, 2) ART-naïve or clinically indicated to change ART treatments, and 3) aged 16 or older. Due to their dual enrollment in the randomized controlled trial, women also were required to have access to a cell phone and be willing to receive text messages. Eligible women who agreed to participate provided written informed consent. A total of 119 women living with HIV were enrolled from June 2016 to December 2017.

Participants completed an interviewer-administered baseline survey in a confidential office at the study site clinic with the assistance of a tablet. All measures were translated into Kiswahili. Following the baseline visit, participants returned monthly for ART refills and adherence checks; viral load was measured at baseline, 3- and 6-months after baseline. Participants received 250 KSh (approximately $2.50 USD) to compensate for their transportation and time at each study visit.

All research procedures were approved by the Human Subjects Research Committee of the University of Washington, Seattle, USA and by the Kenyatta National Hospital - University of Nairobi Ethics and Research Committee in Nairobi, Kenya.

Assessment and Measures

The assessment was administered at the baseline of the randomized controlled trial when women were initiating ART. The assessment was split into two sections: A) the individual-level assessment, where participants were asked questions about themselves in a survey, and B) the network-level assessment, where participants listed alters and responded to questions about each alter using an adaptive, open-source software package called EgoWeb (Sourceforge, Inc).

During the individual-level assessment, participants were asked to respond to standard socio-demographic questions including their age; religion; marital status; level of education; and financial wellbeing, including whether they had enough money to buy airtime, food, and basic necessities, and whether they were worried about finances or had difficulty affording or traveling to access health care. A principle components analysis reduced the large set of finance variables to a single variable that contains most of the information of the larger set of variables (Campbell & William, 1981).

They were also asked to respond to conventional, individual-level measures of social support and stigma:

Individual-level social support was assessed using the 19-item *Medical Outcomes Study Social Support Survey (MOS-SSS)* (Sherbourne & Stewart, 1991), which included subscales that addressed educational/informational, tangible, and affectionate support, and positive social interaction. Each question (e.g. How often do you have "someone you can count on to listen when you need to talk" or "someone to take you to the doctor if you needed it"), has a response scale of 1 (*none of the time*) to 5 (*all of the time*; $\alpha = 0.98$) The raw total score was transformed to a 0-100 scale, with higher values representing more social support. The MOS-SSS has been validated among people living with HIV in SSA (Abrefa-Gyan, Cornelius, & Okundaye, 2015; Gaede et al., 2006).

Individual-level stigma was assessed using the *Internalized AIDS-Related Stigma Scale (IA-RSS)*, a 6-item measure assessing one's self-defacing beliefs and negative perceptions of people living with HIV/AIDS (e.g. "I sometimes feel worthless because I am HIV positive" and "It is

difficult to tell people about my HIV infection"; Kalichman et al., 2008). Response options range from 1 *(strongly disagree)* to 4 *(strongly agree).* Scores for individual items were then averaged to provide a mean score, ranging from 1-4, with higher scores corresponding to increased endorsement of internalized AIDS-related stigma. The IA-RSS was developed through data collected from a convenience sample of PLWH in South Africa, Swaziland and the United States and is internally consistent in our sample ($\alpha = 0.78$).The IA-RSS has been utilized among people living with HIV in SSA (Bogart et al., 2015; Kamen et al., 2015; Tsai, 2015).

The network-level assessment followed a protocolized personal network name generation methodology to prompt participants to name up to 20 individuals, referred to as alters, they had contact with in the past six months (Bogart et al., 2015). Despite variation in each participant's network size, evidence supports that a sample of up to 20 alters sufficiently captures the structural and compositional variability present in most personal networks (McCarty, Killworth, & Rennell, 2007).

After obtaining the list of alters, study staff asked each participant questions about each alter. Network structure was assessed by the number of alters and density, which was assessed by probing whether each unique pair of alters knew each and how frequently they communicated. Network characteristics described the relationships between the participant and the alter and the qualities of each alter. In addition to reporting basic socio-demographics about each alter (including alters' age, gender, relationship with the participant), participants were also asked to describe how frequently they interacted with each alter, and how close they considered their relationship. We also asked whether the participant had disclosed their HIV status and engagement in sex work. Network-level variables were calculated as indices of simple ratios based on each participant's network size as the denominator and a count of various subgroups as the numerator. Variables were calculated at the alter level before being aggregated to the participant level.

To measure network-level social support, study staff asked questions about the provision and receipt of social support from each alter: (1) "How often do the following people help and support you, either by providing emotional support, information, or something tangible like a ride to the clinic or a place to stay?", and (2) "How often do you provide help and support, either by providing emotional support, information, or something tangible like money or a place to stay, to the following people?*"* Each item was scored on a four-point scale from 0 (*rarely*) to 3 (*often*). These questions were utilized in a prior survey (Bogart et al., 2015) and were edited with the study team prior to implementation.

To assess network-level stigma, we asked: 1) "In this list of people [you previously identified as knowing your HIV status], how would you describe their response to knowing you are HIV-positive?" (Answer options: stigmatizing, stigmatizing and supportive, supportive), 2) "Have you not told the following people [you previously reported did not know your HIV status] because you fear their reaction?", and 3) "Who do you think holds the opinion that 'Most people with HIV are responsible for having their illness?'" Each item was dichotomized as 1 (*any endorsement of stigma/yes*) or 0 (*no endorsement of stigma/no*).

We also created a composite network-level social support and stigma (SSS) variable. We developed two versions of network-level social support and stigma based on the network data: Social Support A: amount of support received from alter; Social Support B: stipulations from "Social Support A" and amount of support provided to alters; Stigma A: alter responded to HIV disclosure in a stigmatizing manner or alter was perceived as believing that individuals with AIDS were responsible for their illness; Stigma B: stipulations in "Stigma A" or participant did not disclose HIV status to the alter because of a feared reaction.

Measurement of outcome variables**.** The primary outcome variable was dichotomous viral suppression, operationalized as $\leq$30 copies/mL six months after ART initiation.

ART adherence data were collected monthly using a self-reported, validated visual analogue scale (VAS) and refill timing (Lu et al., 2008; Oyugi et al., 2004). We dichotomously coded self-reported VAS medication adherence as "perfect" (missing no doses) or "imperfect" (missing any doses; dichotomous, monthly). These methods of adherence and variable formulation have been used to assess adherence in previous studies conducted at the Ganjoni Clinic (Graham et al., 2012; Graham et al., 2010). Second, refill timing was dichotomized as "good" if participants were no more than 48 hours late to their six-month appointment and ART refill, versus "late" if they came more than 48 hours after they would have run out of ART. This 48-hour threshold was selected as it is the shortest time period after which recurrent viremia could occur (Graham et al., 2012).

Analysis Plan

For the first set of analyses, we used a subsample of participants with complete data on the variables in each test (with resulting subsamples varying from 94-119 participants). We conducted univariate analyses to understand demographic characteristics of the sample and bivariate analyses to assess how these characteristics differed between women who engaged in sex work and women who did not engage in sex work. We then examined individual-level social support and stigma and conducted bivariate tests to assess their relationship with viral suppression and ART adherence.

Second, we characterized network-level variables with univariate analyses and conducted bivariate analyses to describe the relationship between network-level variables and viral suppression and ART adherence.

Third, we used multiple logistic regression to assess the impact of the individual- and network-level social support and stigma variables on viral suppression and ART adherence. For social support and suppression, we proposed to conduct a mediation analysis to determine whether network-level measures mediated the relationship between the associated individual-level measure and both viral suppression and ART adherence. If association between the individual measure and

viral suppression or ART adherence were present, we propose to test a model of mediation (MacKinnon, 2008). The mediated effect and its confidence interval would be obtained using bootstrap resampling (Shrout & Bolger, 2002). In the absence of a direct effect between the individual measure and viral suppression or ART adherence, it would not be necessary to further examine mediation.

Fourth, in order to assess the relative impact of social support and stigma at the network-level, we used multiple imputation to account for missing data. Specifically, 24 participants (21%) were missing the primary outcome variable of month six viral load data; 12 were lost to follow up, 1 passed away and 12 viral load tests were compromised. According to our *a priori* plan for missing data, we considered those who were lost to follow-up as detectable at month six. In order to include these participants in the analyses, we conducted multiple imputation to assign values for missing data based on time-invariant demographic characteristics and variables included in our model (Blackwell, Honaker & King, 2017). Subsequent analyses were then conducted within the imputed datasets.

Next, in order to characterize network-level social support and stigma, we created a composite "social support and stigma" (SSS) variable, which is a weighted linear combination of social support and stigma, adjusted by the amount of contact the participant had with each alter. First, the social support and stigma scores were standardized. We conducted an iterative grid search to determine the appropriate weight to combine the standardized stigma score with the standardized social support score, and evaluated the four potential combinations of the versions of SSS to identify the combination of weight and stigma and support versions that was most predictive in cross-validation. These alter-level social support-stigma scores were then summed to create one SSS score per participant.

Finally, we assessed the impact of SSS on viral suppression. We conducted multiple logistic regression, adjusting for intervention condition, number of alters, and personal finances. To improve interpretation of SSS, we simulated counterfactual scenarios to assess the relative impact of stigma

and social support on viral suppression. Counterfactual scenarios represent possible combinations of stigma and support which are not observed in the data, but that improve the ability to detect meaningful effects of the observed data. Expected probabilities and first differences were used to determine how the counterfactual scenarios would impact viral suppression.

Results

Participant Flow

A total of 119 participants were enrolled at baseline and 106 participants were retained at month six; 12 participants were lost to follow up and one participant died. An additional 12 VL tests at month six were compromised for participants who were retained in care. Thus, the preliminary analyses included data on 106 participants.

Outcome variables

At month six, 65% (69/106) participants had achieved viral suppression.
All but three participants (97%, 94/97) came for their appointment within 2 days of their last prescribed dose and thus had "good" refill timing; 83.5% reported having perfect adherence on the VAS.

Individual-level descriptive data

Sociodemographic data is described in Table 1. The final sample of 119 participants ranged in age from 21 to 59 years old (*M/SD* = 38.13/8.82) at baseline and the majority (81%) reported engaging in sex work. Over three quarters of the participants (78%) reported having someone close to them die of HIV/AIDS. Overall, participants were predominantly Christian (80%) and most participants had only completed primary education (62%). While the majority of participants reported having some form of employment excluding sex work (59%), the participants reported having

substantial financial difficulties. For example, the majority (77%) reported experiencing at least some difficulty affording basic necessities and 80% reported concern about money for at least several days in the past two weeks.

There were some sociodemographic differences between participants who reported engaging in sex work and those who did not. Compared to participants who did not engage in sex work, participants who engaged in sex work were less educated (33% vs 7%, p=0.001) and were more likely to be widowed or divorced (25% versus 44%, p=0.02). Participants who engaged in sex work were also more likely to report having sold items to afford healthcare expenses (4% versus 43%, p=0.001) and, despite not living any further away, were more likely to have difficulty affording transportation expenses for clinic appointments (21% versus 50%, p=0.02).

Individual-level social support and stigma effects on viral suppression and ART adherence

Overall, the individual-level MOS Social Support Scale showed mid-range levels of overall support (*M/SD*=64.9/26.5, possible range 0-100), with emotion and tangible support higher than subscales for both affective support and positive social interaction (Table 2). Participants scored mid-range levels of individual-level stigma on the Internalized AIDS-related Stigma scale (*M/SD* = 3.45/1.72, possible range 1-6).

The MOS Social Support Scale and Internalized AIDS-related Stigma scores did not differ significantly between participants who were virally suppressed and those who had a detectable viral load at month six (p=0.62). Participants who were virally detectable reported a MOS Social Support score of 68% compared to 65% among participants who were virally suppressed. Although not statistically significant, participants who were virally detectable experienced slightly less internalized AIDS-related stigma compared to participants with a detectable viral load (3.1 versus 3.6, p=0.28).

Network-level descriptive data: network structure and network characteristics

On average, participants reported a total of 12 alters in their networks (*SD* = 2.02) and about half of alters knew each other, suggesting relatively dense networks (*M/SD*=.49/0.27)

Network characteristics are presented in Table 3. Forty-percent of the alters were family members, 12% were romantic partners or clients, 26% were co-workers or friends, 2% were heath providers or religious leaders, and 20% were characterized as "other". The average age of alters was slightly lower than the average age of the participants (35.1 versus 38.13 years) and more network members were female and Christian. While participants had talked with 38% of their alters about HIV, participants had overall low rates of HIV disclosure (15%) and reported avoiding disclosure was avoided for all but three of the remaining alters for fear of their reaction (100%). Participants generally had contact with their alters twice a week and reported having close relationships with 58% of their alters. Participants provided and received high levels of social support and financial support.

Network-level social support and stigma effects on viral suppression and ART adherence

There were few statistically significant network-level differences between participants who were virally suppressed and those who had a detectable viral load. Participants with a detectable viral load were less likely to have disclosed about their engagement in sex work (6% versus 41%, $p<0.001$) and had more alters who were Christian (92% versus 78%, $p=0.02$).

Bivariate analyses were conducted for network characteristics of perfect versus imperfect self-reported adherence on the VAS at month six (Table 4). Participants who reported having imperfect adherence at month six reported having more alters with stigmatizing attitudes about sex work compared to participants who did not report perfect adherence (*M/SD*= 40.00/45.95 versus 12.52/30.33, $p=0.02$) and had less contact with their alters (*M/SD* = 2.84/1.15 versus 3.26/0.64, $p=0.04$, possible range = 0-4).

Although only three participants had late refill timing at month six, there were several differences distinguishing them from the participants with good refill timing (Table 5). Participants

with late refill timing were younger (*M/SD* = 24.62/10.63 versus 34.37/7.32, *p*=0.028), had a higher percentage of alters who were sex partners (*M/SD* = 35.71/13.27 versus 13.00/14.49, *p*=0.01), and were more likely to have alters who held stigmatizing beliefs towards PLWH (*M/SD* = 35.71/12.37 versus 11.79/20.90, *p*=0.05), compared to participants with good refill timing. While not statistically significant, participants with late refill timing were more likely to have disclosed to their alters about their engagement in sex work (*M/SD* = 65.87/15.12 versus 34.67/31.11, *p*=0.09) and were more likely to receive financial support from their alters (*M/SD* = 79.37/11.00 versus 49.40/27.99, *p*=0.07), compared to participants with late refill timing.

Multiple Logistic Regression Analyses: The effect of individual- and network-level social support and stigma on viral suppression and ART adherence

In multiple logistic regression models, neither individual- nor network-level social support and support variables had a statistically significant effect on viral suppression or perfect VAS adherence (Tables 6 & 7). No analysis was conducted with refill timing because of the small number of participants with late refill timing.

Additionally, we tested two mediation model to assess whether the network-level social support and stigma variables mediated the relationship between individual-level endorsements of either social support or stigma, and viral suppression. We found no evidence of mediation for either social support or stigma. (Data not shown.)

Relative Effect of Social Support and Stigma (SSS) on Viral Suppression

The iterative grid search found that the combination of Social Support B and Stigma A, with Stigma A weighted 4 times more than Social Support B best predicted viral suppression in a 5-fold cross-validation.

Following multiple imputation, our analyses proceeded examining viral suppression. In our model with age, personal finances, sex worker status, number of alters, and intervention condition, SSS had a negative but nonsignificant effect on viral suppression.

For counterfactuals, we held covariates equal to the mean and varied counterfactuals of the SSS variable. These comparisons were set to mimic typical levels of SSS in the sample. It was not sufficient to increase or decrease SSS by standard deviation, which would have aggregated over all changes in social support and stigma. We simulated counterfactuals within a network size of 12 alters, which was the mean in our sample.

In order to compare the relative impact of social support and stigma at the alter level, we created two simulated clusters of scenarios. In the first cluster, we assumed all 12 alters were not stigmatizing and changed the number of alters that were also supportive within the network. The "very low support" scenario included 9 supportive alters, the "low support" scenario included 10 supportive alters, the "mean support" included 11 supportive alters, and the "high support" included all 12 supportive alters. Examining expected probabilities (Figure 1) and first differences (Figure 2) highlighted that adding more supportive alters had little effect on the probability of viral suppression. There was a 0.675 probability of achieving viral suppression with 12 supportive alters compared to a 0.673 probability 9 supportive alters; the difference was nonsignificant.

In the second cluster, we examined the impact of adding stigmatizing alters. In all scenarios, we assumed that all 12 alters provided a high level of support and then simulated the effect on the probability of viral suppression when some of those alters also provided stigma. The "very low stigma" scenario included no stigmatizing alters, the "low stigma" scenario included 1 stigmatizing alter, the "mean stigma" scenario included 2 stigmatizing alters, and the "high stigma" scenario included 3 stigmatizing alters. Examining expected probabilities (Figure 3) and first differences (Figure 4) highlighted that adding more stigmatizing alters had a small effect on the probability of

viral suppression. There was a 0.68 probability of achieving viral suppression with 0 stigmatizing alters compared to a 0.66 probability 3 stigmatizing alters; the difference was nonsignificant.

Discussion

In this study, we examined how individual- and network-level measures of social support and stigma impacted viral suppression and ART adherence among women living with HIV in Mombasa, Kenya. Results did not lend support for our hypothesis that social support and stigma would be significantly associated with viral suppression at the individual level. This is surprising given the breadth of research demonstrating that social support (Croome et al., 2017) and stigma (Shubber et al., 2016) are associated with viral suppression and ART adherence. One possible explanation was that the women received support and stigma from the same alters, thus negating the net effect on viral suppression.

We conducted additional comparisons of the relative impact of social support and stigma at the alter level based on our network-level data. This was a critical step, because our population of PLWH in SSA is both highly stigmatized and resource constrained. Participants may rely on specific alters for financial and social support, making it difficult to remove themselves from these relationships even if they fear stigma. Thus, our participants may be particularly likely to simultaneously experience stigma and receive support from the same alters. Stigma and social support have opposite effects on viral suppression in the literature. Therefore, the two effects could counteract each other and blunt or eliminate any relationship between social support and stigma on ART adherence and viral suppression. Network analysis collects data at the level of the alter, which allows these relationships to be examined both independently and in conjunction. Despite the importance of network analysis, very few studies have looked at the effect of network-level characteristics on viral suppression (Bogart et al., 2018; Ghosh et al., 2017).

Our network analysis strategy allowed us to test relationships between support and stigma and their cumulative association with the probability of viral suppression and ART adherence, even when an alter provided both social support and stigma. We found that although there was low overall endorsement, the stigma from alters was a more powerful influence on viral suppression than social support from alters. Indeed, the best predicting model necessitated that stigma be weighted four times more than social support.

Moreover, counterfactual scenarios indicated that adding one stigmatizing alter had more of an impact on the probability of viral suppression than subtracting one supportive alter. The finding that one stigmatizing alter could have a larger impact on health behavior replicated research demonstrating that participants who perceived stigmatizing beliefs in one alter, especially in a more dense network, were more likely to engage in high risk sexual behavior (Wagner et al., 2015).

To our knowledge, this is the first paper to analyze the relative impact of network-level support and stigma on viral suppression. Only one other paper has examined the relationship of both social support and stigma at the network level, using ART adherence as an outcome. The study, conducted in a longitudinal cohort of 221 PLWH, found that network-level social support (frequency of contact with alters), but not individual-level support buffered the relationship between stigma and ART adherence (Bogart et al., 2015). Our findings run in contrast to this research, because of the minimal effects of added social support relative to stigma.

Overall disclosure of HIV serostatus to alters was low (Evangeli & Wroe, 2017), and there was no difference in disclosure based on viral suppression status. However, among participants who engaged in sex work, those who had disclosed their involvement in sex work to a higher percentage of alters were significantly more likely to be virally suppressed. While there is a wealth of literature regarding impacts of HIV disclosure on health outcomes (Evangeli & Wroe, 2017), understanding why viral suppression is associated with disclosure of sex work status but not HIV serostatus could

inform our understanding of barriers to achieving viral suppression and may open avenues for intervention development. For example, it is possible that comfort sharing involvement in sex work is a proxy for trust and closeness within a network, and these relationships may be protective. Alternatively, disclosure about engagement in sex work could allow supportive members in their network to provide more support in accessing health care services.

More network differences became apparent when comparing women who reported perfect VAS adherence and had good refill timing. While viral suppression is the gold standard for HIV treatment outcomes (UNAIDS, 2016), self-reported adherence and refill timing seemed to highlight participants with progressively less self-efficacy in HIV care. For example, in our sample, participants who did not report confidently that they had taken their ART adherently were more likely to report experiencing stigma related to sex work and had less contact with their alters. Participants with late refill timing also had many significant differences in network qualities compared to those with good refill timing, including reporting that more alters in their network held stigmatizing attitudes towards PLWH. Individual-level measures of stigma did not capture a statistically significant difference between those with late and good refill timing, highlighting the importance of considering network-level assessments to identify women who could be non-adherent to ART.

The present study has several limitations. Because we asked questions about each alter in the network section, we had to limit the number of items used to capture complex constructs of support and stigma to minimize collection burden. While we solicited input from the study team to identify their perception of the most meaningful items, some of the nuance of the original measures may have been lost. It was also difficult to conduct a direct comparison between the individual-level measures and network-level measures because the specific questions were different. Future iterations may

consider drawing network-level items directly from a validated scale to facilitate accurate comparison.

Second, our analyses were limited by a small sample size which may have hindered our ability to achieve statistical significance despite the presence of a main effect. Future studies could collect data from larger samples or include longitudinal data to improve statistical power.

Third, we did not require participants to list 20 alters (as did Bogart et al; 2015) which may have resulted in reduced endorsement of experiences of stigma. For example, a participant could have reported smaller network size as a result of either having a small network or having only a few people who provide support, or as a result of the loss of alters subsequent to either a disclosure reaction or the ego's perceived stigma. This did, however, allow us to use network size as a variable to describe network structure as participants with stigmatizing alters may have reported smaller network sizes. Future longitudinal studies among women newly initiating ART could examine whether network sizes change over time.

Finally, egocentric social network methodologies rely on self-report from study participants and do not directly assess alter characteristics from network members. However, research suggests there are few differences between ego- and alter-reports of alter behavior, and that ego-reports can be valid for key alter characteristics including HIV-status and relationships between network members (Green et al., 2013). Additionally, just as perceived norms have been shown to relate to HIV risk behaviors, perceived beliefs about stigma and support by alters may be as important as the actuality.

The present study has implications for research on the measurement of social support and stigma, especially among stigmatized populations. Future studies could further explore types of stigma and social support. For example, it may be interesting to look at the relative impact of stigma related to sex work versus related to HIV status, and the impact of stigma that results in discrimination versus stigma that has less overt manifestations. Additionally, future work could examine different types of social support at the network level, such as financial versus emotional

support. Future qualitative research could seek women's perspectives on the complex relationships with alters that provide both social support and stigma, and therefore improve quantitative measurement of their potential effects on viremia.

While collecting network data can be cumbersome, the granular-level data can bring to light the underlying processes influencing health outcomes and consequently highlight novel avenues of intervention. The results presented here suggest that intervening at the network level, for example, by reducing contact with alters who are perceived to be stigmatizing may increase the probability of achieving viral suppression. More interventions are needed to cope with stigma, although this is a notoriously difficult construct to shift (Rao, 2018; Stangl, 2013). While the quality of stigma-reduction interventions has improved, many are only marginally effective, at best (Rao, 2018; Stangl, 2013). There is a need to understand how individual and network variables transact, before expecting strong effects of intervention that try to leverage reductions on just one or the other. Future research could try to replicate this approach in a larger sample to better understand whether or not intervening on individual- or network-level factors or both is really necessary to make a dent toward stigma reduction. As the world strives toward achieving the 95-95-95 goals, an appreciation of these factors will hopefully inform ways to enable more supportive and less stigmatizing attitudes toward among this marginalized group of women, and contribute to their health and well-being.

References

Abrefa-Gyan, T., Cornelius, L., & Okundaye, J. (2015). Gender and Children as the Moderators of the Relationship between Social Support and Quality of Life: An Empirical Study of People Living with HIV/AIDS in Ghana. *Social Work in Public Health*, *30*(7), 550–558. doi:10.1080/19371918.2015.1071611

Atukunda, E. C., Musiimenta, A., Musinguzi, N., Wyatt, M. A., Ashaba, J., Ware, N. C., & Haberer, J. E. (2016). Understanding Patterns of Social Support and Their Relationship to an ART Adherence Intervention Among Adults in Rural Southwestern Uganda. *AIDS & Behavior, 21*(2), 428–440. http://doi.org/10.1007/s10461-016-1559-7

Barroso, J., Leblanc, N. M., & Flores, D. (2017). It's Not Just the Pills: A Qualitative Meta-Synthesis of HIV Antiretroviral Adherence Research. *Journal of the Association of Nurses in AIDS Care*. doi:10.1016/j.jana.2017.02.007

Blackwell, M., Honaker, J., & King, G. (2017). A unified approach to measurement error and missing data: overview and applications. *Sociological Methods & Research, 46*(3), 303-341. doi:10.1177/0049124115585360

Bangsberg, D. R. (2006). Less Than 95% Adherence to Nonnucleoside Reverse-Transcriptase Inhibitor Therapy Can Lead to Viral Suppression. *Clinical Infectious Diseases, 43*(7), 939–941. http://doi.org/10.1086/507526

Bogart, L. M., Wagner, G. J., Green, H. D., Mutchler, M. G., Klein, D. J., & McDavitt, B. (2015). Social Network Characteristics Moderate the Association Between Stigmatizing Attributions About HIV and Non-adherence Among Black Americans Living with HIV: a Longitudinal Assessment. *Annals of Behavioral Medicine*, *49*(6), 865–872. doi:10.1007/s12160-015-9724-1

Bogart, L. M., Mosepele, M., Phaladze, N., Lekoko, B., Klein, D. J., MacCarthy, S., & Green Jr, H. D. (2018). A social network analysis of HIV treatment partners and patient viral suppression in Botswana. *Journal of Acquired Immune Deficiency Syndromes, 78*(2), 183-192. doi:10.1097/QAI.0000000000001661.

Bogart, L. M., Cowgill, B. O., & Kennedy, D. (2008). HIV-related stigma among people with HIV and their families: A qualitative analysis. *AIDS & Behavior*, *12*, 244–254.

Borgatti, S. P. (2005). Centrality and network flow. *Social Networks*, *27*(1), 55–71. doi:10.1016/j.socnet.2004.11.008

Borgatti, S. P. (2006). Identifying sets of key players in a social network. *Computational & Mathematical Organization Theory*, *12*(1), 21–34. doi:10.1007/s10588-006-7084

Borgatti, S. P., & Everett, M. G. (2006). A Graph-theoretic perspective on centrality. *Social Networks*, *28*(4), 466–484. doi:10.1016/j.socnet.2005.11.005

Borgatti, S. P., Carley, K. M., & Krackhardt, D. (2006). On the robustness of centrality measures under conditions of imperfect data. *Social Networks*, *28*(2), 124–136. doi:10.1016/j.socnet.2005.05.001

Campbell, N. A., & Atchley, W. R. (1981). The geometry of canonical variate analysis. *Systematic Biology*, *30*(3), 268-280.

Cohen, S. (2004). Social relationships and health. *American Psychologist, 59*(8), 676. doi:10.1037/0003-066X.59.8.676.

Croome, N., Ahluwalia, M., Hughes, L. D., & Abas, M. (2017). Patient-reported barriers and facilitators to antiretroviral adherence in sub-Saharan Africa. *AIDS*, *31*(7), 995–1007. doi:10.1097/QAD.0000000000001416

El-Bassel, N., Gilbert, L., Wu, E., & Chang, M. (2006). A Social Network Profile and HIV Risk Among Men on Methadone: Do Social Networks Matter? *Journal of Urban Health*, *83*(4), 602–613. doi:10.1007/s11524-006-9075-0

Eshun-Wilson, I., Rohwer, A., Hendricks, L., Oliver, S., & Garner, P. (2019). Being HIV positive and staying on antiretroviral therapy in Africa: A qualitative systematic review and theoretical model. *PloS one, 14*(1), e0210408. doi:10.1371/journal.pone.0210408

Evangeli, M., & Wroe, A. L. (2017). HIV disclosure anxiety: A systematic review and theoretical synthesis. *AIDS & Behavior, 21*(1), 1-11. doi: 10.1007/s10461-016-1453-3.

Everett, M., & Borgatti, S. P. (2005). Ego network betweenness. *Social Networks*, 27(1), 31–38. doi:10.1016/j.socnet.2004.11.007

Gaede, B., Majeke, S., Modeste, R. R. M., Naidoo, J. R., Titus, M. J., & Uys, L. R. (2006). Social support and health behaviour in women living with HIV in KwaZulu-Natal. *SAHARA-J: Journal of Social Aspects of HIV/AIDS*, *3*(1), 362–368. doi:10.1080/17290376.2006.9724862

Ghosh, D., Krishnan, A., Gibson, B., Brown, S. E., Latkin, C. A., & Altice, F. L. (2017). Social network strategies to address HIV prevention and treatment continuum of care among at-risk and HIV-infected substance users: a systematic scoping review. *AIDS & Behavior*, *21*(4), 1183-1207. doi: 10.1007/s10461-016-1413-y.

Gilbert, Leah, & Walker, L. (2010). “My biggest fear was that people would reject me once they knew my status…”: stigma as experienced by patients in an HIV/AIDS clinic in Johannesburg, South Africa. *Health & Social Care in the Community, 18*(2), 139–146. doi:10.1111/j.1365-2524.2009.00881.x

Graham, S. M., Micheni, M., Secor, A., van der Elst, E. M., Kombo, B., Operario, D., ... &

Simoni, J. M. (2018). HIV care engagement and ART adherence among Kenyan gay, bisexual, and other men who have sex with men: a multi-level model informed by qualitative research. *AIDS Care*, 30(sup5), S97-S105. doi:10.1080/09540121.2018.1515471

Graham, S. M., Jalalian-Lechak, Z., Shafi, J., Chohan, V., Deya, R. W., Jaoko, W., ... & McClelland, R. S. (2012). Antiretroviral treatment interruptions predict female genital shedding of genotypically resistant HIV-1 RNA. *Journal of Acquired Immune Deficiency Syndromes*, 60(5), 511. doi:0.1097/QAI.0b013e31825bd703

Graham, S. M., Masese, L., Gitau, R., Jalalian-Lechak, Z., Richardson, B. A., Peshu, N., ... & Overbaugh, J. (2010). Antiretroviral adherence and development of drug resistance are the strongest predictors of genital HIV-1 shedding among women initiating treatment. *Journal of Infectious Diseases*, 202(10), 1538-1542. doi:10.1086/656790

Green Jr, H. D., Hoover, M. A., Wagner, G. J., Ryan, G. W., & Ssegujja, E. (2014). Measuring agreement between egos and alters: Understanding informant accuracy in personal network studies. *Field Methods*, *26*(2), 126-140. doi:10.1177/1525822X13492676

Kalichman, S. C., Simbayi, L. C., Cloete, A., Mthembu, P. P., Mkhonta, R. N., & Ginindza, T. (2008). Measuring AIDS stigmas in people living with HIV/AIDS: the Internalized AIDS-Related Stigma Scale. *AIDS Care, 21*(1), 87–93. doi:10.1080/09540120802032627

Kamen, C., Arganbright, J., Kienitz, E., Weller, M., Khaylis, A., Shenkman, T., et al. (2015). HIV-related stigma: implications for symptoms of anxiety and depression among Malawian women. *African Journal of AIDS Research*, *14*(1), 67–73. doi:10.2989/16085906.2015.1016987

Kaufman, M. R., Cornish, F., Zimmerman, R. S., & Johnson, B. T. (2014). Health Behavior Change Models for HIV Prevention and AIDS Care: Practical Recommendations for a

Multi-Level Approach. *Journal of Acquired Immune Deficiency Syndromes*, 66, S250–S258. http://doi.org/10.1097/QAI.0000000000000236

Knowlton, A. R., Yang, C., Bohnert, A., Wissow, L., Chander, G., & Arnsten, J. A. (2011). Informal Care and Reciprocity of Support are Associated with HAART Adherence Among Men in Baltimore, MD, USA. *AIDS & Behavior, 15*(7), 1429–1436. http://doi.org/10.1007/s10461-010-9749-1

Latkin, C. A., Forman, V., Knowlton, A., & Sherman, S. (2003). Norms, social networks, and HIV-related risk behaviors among urban disadvantaged drug users. *Social Science & Medicine*, *56*(3), 465–476. doi:10.1016/S0277-9536(02)00047-3

McCarty, C., Killworth, P. D., & Rennell, J. (2007). Impact of methods for reducing respondent burden on personal network structural measures. *Social Networks*, *29*(2), 300–315. doi:10.1016/j.socnet.2006.12.005

Lu M, Safren SA, Skolnik PR, Rogers WH, Coady W, Hardy H, Wilson IB. (2008). Optimal recall period and response task for self-reported HIV medication adherence. *AIDS & Behavior*. 12(1):86-94. doi:10.1007/s10461-007-9261-4

MacKinnon, D. P. (2008). Multivariate applications series. Introduction to statistical mediation analysis. New York, NY: Taylor & Francis Group/Lawrence Erlbaum Associates.

Oyugi, J. H., Byakika-Tusiime, J., Charlebois, E. D., Kityo, C., Mugerwa, R., Mugyenyi, P., & Bangsberg, D. R. (2004). Multiple validated measures of adherence indicate high levels of adherence to generic HIV antiretroviral therapy in a resource-limited setting. *Journal of Acquired Immune Deficiency Syndromes,* 36(5), 1100-1102.

Ramjee, G., & Daniels, B. (2013). Women and HIV in sub-Saharan Africa. *AIDS Research and Therapy*, *10*(1), 30. doi:10.1186/1742-6405-10-30

Rao, D., Desmond, M., Andrasik, M., Rasberry, T., Lambert, N., Cohn, S. E., & Simoni, J. (2012). Feasibility, acceptability, and preliminary efficacy of the unity workshop: an internalized stigma reduction intervention for African American women living with HIV. *AIDS Patient Care and STDs*, *26*(10), 614-620. doi:10.1089/apc.2012.0106

Remien, R. H., Bastos, F. I., Terto Jnr, V., Raxach, J. C., Pinto, R. M., Parker, R. G., et al. (2007). Adherence to antiretroviral therapy in a context of universal access, in Rio de Janeiro, Brazil. *AIDS Care, 19*(6), 740–748. doi:10.1080/09540120600842516

Sherbourne, C. D., & Stewart, A. L. (1991). The MOS social support survey. *Social Science & Medicine, 32*(6), 705–714. doi:10.1016/0277-9536(91)90150-B

Shrout, P.E. & Bolger, N. (2002) Mediation in experimental and nonexperimental studies: new procedures and recommendations. *Psychological Methods, 7*(4), 422-445.

Shubber, Z., Mills, E. J., Nachega, J. B., Vreeman, R., Freitas, M., Bock, P., et al. (2016). Patient-Reported Barriers to Adherence to Antiretroviral Therapy: A Systematic Review and Meta-Analysis. *PLOS Medicine*, *13*(11), e1002183. doi:10.1371/journal.pmed.1002183

Sourceforge, Inc. (n.d.). Egonet. Bellingham. Retrieved from http://sourceforge.netprojectsegonet

Stangl, A. L., Lloyd, J. K., M Brady, L., Holland, C. E., & Baral, S. (2013). A systematic review of interventions to reduce HIV-related stigma and discrimination from 2002 to 2013: how far have we come? *Journal of the International AIDS Society, 16*(3(Suppl 2)). doi:10.7448/IAS.16.3.18734

Tsai, A. C. (2015). Socioeconomic Gradients in Internalized Stigma Among 4,314 Persons with HIV in Sub-Saharan Africa. *AIDS & Behavior*, *19*(2), 270–282. doi:10.1007/s10461-014-0993-7

UNAIDS. (2016a) Resolution No A/RES/70/266, Political Declaration on HIV and AIDS: On the Fast-Track to Accelerate the Fight against HIV and to End the AIDS Epidemic by 2030 2016 [25 January 2017]. Available from: http://www.unaids.org/sites/default/files/media_asset/2016-political-declaration-HIV-AIDS_en.pdf

UNAIDS. (2016b). Prevention Gap Report. Retrieved from http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf

Wills, T. A., Ainette, M. G., Baum, A., Revenson, T. A., & Singer, J. (2012). Social networks and social support. *Handbook of Health Psychology*, 465.

Wu, F., He, X., Guida, J., Xu, Y., & Liu, H. (2015). Network stigma towards people living with HIV/AIDS and their caregivers: An egocentric network study. *Global Public Health*, *10*(9), 1032–1045. doi:10.1080/17441692.2014.1003572

Table 1. Socio-demographics by sex worker status among Kenyan women living with HIV

	Overall (n=119)	Sex worker (n=96)	Non-sex worker (n=23)	p-value
Age (mean (SD))	38.13 (8.82)	38.27 (8.63)	37.58 (9.74)	0.734
Education (%)				0.001
Did not complete primary	19 (16.0)	15 (15.8)	4 (16.7)	
Completed primary	74 (62.2)	66 (69.5)	8 (33.3)	
Completed secondary	11 (9.2)	7 (7.4)	4 (16.7)	
Post-secondary	15 (12.6)	7 (7.4)	8 (33.3)	
Religion (%)				0.022
Christian	96 (80.0)	81 (84.4)	15 (62.5)	
Muslim	22 (18.3)	13 (13.5)	9 (37.5)	
Other	2 (1.7)	2 (2.1)	0 (0.0)	
Travel time to clinic (%)				0.631
0.5 hour	22 (18.3)	19 (19.8)	3 (12.5)	
0.5-1 hour	69 (57.5)	56 (58.3)	13 (54.2)	
1-2 hours	26 (21.7)	19 (19.8)	7 (29.2)	
2+ hours	3 (2.5)	2 (2.1)	1 (4.2)	
Job (outside of sex work) (%)				<0.001
Working full-time	47 (39.8)	34 (35.8)	13 (56.5)	
Working part-time	23 (19.5)	21 (22.1)	2 (8.7)	
No other employment	41 (34.7)	40 (42.1)	1 (4.3)	
Marital Status (%)				0.02
Single	31 (25.8)	27 (28.1)	4 (16.7)	
Partnered	41 (34.2)	27 (28.1)	14 (58.3)	
Widowed/Divorced	48 (40.0)	42 (43.8)	6 (25.0)	
Children (mean (SD))	2.23 (1.48)	2.23 (1.43)	2.21 (1.69)	0.951
Income (%)				0.137
<US$1 per day	11 (9.2)	8 (8.3)	3 (13.0)	
$1–5 per day	66 (55.5)	56 (58.3)	10 (43.5)	
$5–20 per day	39 (32.8)	31 (32.3)	8 (34.8)	
>$20 per day	3 (2.5)	1 (1.0)	2 (8.7)	
Family/friend died of HIV/AIDS = 1 (%)	90 (77.6)	74 (77.9)	16 (76.2)	1
Financial Status - Principle Components	0.00 (1.38)	-0.13 (1.36)	0.51 (1.37)	0.044

Table 2. Bivariate tests of individual-level social support and stigma scores by viral suppression and ART adherence among Kenyan women living with HIV

	Virally Suppressed (n=69)	Virally Detectable (n=37)	*p*-value
MOS Social Support Scale (range 0-100) (mean (SD))	64.53 (28.00)	67.84 (28.26)	0.615
Emotional Support subscale (range 0-100) (mean (SD))	65.22 (35.96)	72.38 (32.86)	0.386
Tangible Support subscale (range 0-100) (mean (SD))	77.26 (27.07)	78.50 (31.72)	0.852
Affective Support subscale (range 0-100) (mean (SD))	59.42 (36.41)	59.67 (37.32)	0.977
Positive Social Interaction subscale (range 0-100) (mean (SD))	55.19 (35.67)	54.67 (35.53)	0.95
Internalized AIDS-related Stigma (range 1-6) (mean (SD))	3.57 (1.73)	3.12 (1.79)	0.277
	Perfect VAS adherence (n=81)	Imperfect VAS adherence (n=16)	*p*-value
MOS Social Support Scale (range 0-100) (mean (SD))	64.12 (27.57)	63.90 (24.22)	0.977
Emotional Support subscale (range 0-100) (mean (SD))	68.17 (35.64)	71.09 (31.82)	0.761
Tangible Support subscale (range 0-100) (mean (SD))	77.16 (27.60)	81.25 (21.29)	0.577
Affective Support subscale (range 0-100) (mean (SD))	55.04 (39.50)	45.83 (34.83)	0.388
Positive Social Interaction subscale (range 0-100) (mean (SD))	50.62 (39.28)	45.31 (29.81)	0.611
Internalized AIDS-related Stigma (range 1-6) (mean (SD))	3.31 (1.71)	2.94 (1.34)	0.416
	Good refill timing (n=94)	Late refill timing (n=3)	*p*-value
MOS Social Support Scale (range 0-100) (mean (SD))	63.75 (27.23)	74.56 (12.15)	0.496
Emotional Support subscale (range 0-100) (mean (SD))	68.28 (35.30)	80.21 (18.04)	0.563
Tangible Support subscale (range 0-100) (mean (SD))	77.53 (26.79)	87.50 (21.65)	0.526
Affective Support subscale (range 0-100) (mean (SD))	53.01 (39.24)	69.44 (9.62)	0.473
Positive Social Interaction subscale (range 0-100) (mean (SD))	49.56 (38.36)	55.56 (9.62)	0.788
Internalized AIDS-related Stigma (range 1-6) (mean (SD))	3.28 (1.64)	2.33 (2.31)	0.335

Table 3. Bivariate tests of network characteristics by HIV viral suppression (≤ 30 copies/mL) six months following ART initiation among Kenyan women living with HIV

	Virally Suppressed (%) (n=69)	Virally Detectable (%) (n=37)	*p*-value
Alter demographics			
Mean age (mean (SD))	32.27 (10.33)	35.15 (11.75)	0.252
Percent Female (mean (SD))	61.91 (14.74)	64.43 (18.77)	0.498
Percent Christian (mean (SD))	78.46 (26.29)	91.81 (14.27)	0.018**
Percent sex partners(mean (SD))	15.35 (13.11)	15.26 (25.31)	0.981
Relationship			
Amount of contact (mean (SD)) (range 0-4)	3.20 (0.70)	3.29 (0.61)	0.581
Very close relationship (mean (SD))	57.61 (26.93)	61.32 (25.83)	0.553
Talked with about HIV (mean (SD))	40.93 (25.72)	35.87 (26.43)	0.405
Disclosure			
Disclosed about sex work (mean (SD))	40.69 (28.24)	5.70 (13.98)	<0.001***
Disclosed HIV status (mean (SD))	14.97 (20.77)	14.33 (20.46)	0.896
Nondisclosure of HIV bc feared reaction (mean (SD))	99.64 (2.79)	100.00 (0.00)	0.564
Stigma			
Experienced stigma about sex work (mean (SD))	13.59 (30.49)	20.00 (44.72)	0.669
Experienced stigma about HIV status (mean (SD))	17.14 (34.93)	0.00 (0.00)	0.085
Stigmatizing attitudes towards PLWH (mean (SD))	12.57 (20.31)	10.45 (22.34)	0.673
Support			
Received social support (mean (SD)) (range 0-3)	1.80 (0.69)	1.94 (0.70)	0.415
Provided social support (mean (SD)) (range 0-3)	2.07 (0.65)	1.99 (0.81)	0.606
Received financial support (mean (SD))	53.65 (26.45)	43.25 (29.44)	0.105
Provided financial support (mean (SD))	59.42 (30.82)	57.70 (33.20)	0.816

Note:*p<0.1; **p<0.05; ***p<0.01

Table 4. Bivariate tests of network characteristics by self-reported ART adherence (perfect VAS adherence versus imperfect VAS adherence) six months following ART initiation among Kenyan women living with HIV

	Perfect VAS adherence (%) (n=81)	Imperfect VAS adherence (%) (n=16)	*p*-value
Alter demographics			
Mean age (mean (SD))	34.20 (7.64)	33.38 (7.39)	0.695
Percent Female (mean (SD))	63.75 (18.06)	59.66 (17.59)	0.407
Percent Christian (mean (SD))	82.52 (25.27)	82.80 (19.82)	0.967
Percent sex partners(mean (SD))	13.53 (15.26)	14.59 (13.48)	0.796
Relationship			
Amount of contact (mean (SD)) (range 0-4)	3.26 (0.64)	2.84 (1.15)	0.039**
Very close relationship (mean (SD))	59.60 (26.17)	61.50 (25.41)	0.79
Talked with about HIV(mean (SD))	39.56 (25.81)	37.80 (24.14)	0.802
Disclosure			
Disclosed about sex work (mean (SD))	35.03 (32.01)	42.59 (25.39)	0.501
Disclosed HIV status (mean (SD))	14.97 (21.34)	16.95 (18.41)	0.753
Nondisclosure of HIV status bc feared reaction (mean (SD))	99.65 (2.74)	100.00 (0.00)	0.635
Stigma			
Experienced stigma about sex work (mean (SD))	12.52 (30.33)	40.00 (45.95)	0.022**
Experienced stigma about HIV (mean (SD))	14.47 (33.26)	24.42 (36.44)	0.409
Stigmatizing attitudes towards PLWH (mean (SD))	12.60 (21.99)	12.28 (16.29)	0.957
Support			
Received Social Support (mean (SD)) (range 0-3)	1.85 (0.68)	2.01 (0.75)	0.412
Provided Social Support (mean (SD)) (range 0-3)	2.07 (0.70)	2.19 (0.63)	0.505
Received financial support (mean (SD))	50.98 (28.72)	47.04 (25.17)	0.611
Provided financial support (mean (SD))	60.80 (32.29)	58.85 (27.50)	0.822

Note:*p<0.1; **p<0.05; ***p<0.01

This table includes data from the 97 participants who reported self-reported VAS data at month six. Reports were dichotomized as “perfect VAS adherence” if they reported 100% adherence (n=81) and “imperfect VAS adherence” (n=16) if they reported anything under 100% adherence.

Table 5. Bivariate tests of network characteristics by ART adherence (good refill timing versus late refill timing) six months following ART initiation among Kenyan women living with HIV

	Good refill timing (%) (n=94)	Late refill timing (%) (n=3)	*p*-value
Alter demographics			
Mean age (mean (SD))	34.37 (7.32)	24.64 (10.63)	0.028**
Percent Female (mean (SD))	63.52 (17.95)	49.21 (13.75)	0.175
Percent Christian (mean (SD))	82.70 (24.67)	78.35 (12.75)	0.763
Percent sex partners(mean (SD))	13.00 (14.49)	35.71 (12.37)	0.009**
Relationship			
Amount of contact (mean (SD)) (range 0-4)	3.25 (0.66)	1.38 (1.40)	<0.001***
Very close relationship (mean (SD))	60.25 (26.19)	49.21 (13.75)	0.47
Talked with about HIV(mean (SD))	39.26 (25.82)	39.68 (5.50)	0.978
Disclosure			
Disclosed about sex work (mean (SD))	34.67 (31.11)	65.87 (15.12)	0.090*
Disclosed HIV status (mean (SD))	15.05 (20.91)	33.33 (NA)	NA
Nondisclosure of HIV status bc feared reaction (mean (SD))	99.70 (2.53)	100.00 (0.00)	0.84
Stigma			
Experienced stigma about sex work (mean (SD))	16.45 (35.04)	33.33 (28.87)	0.417
Experienced stigma about HIV status (mean (SD))	17.45 (34.56)	0.00 (0.00)	0.391
Stigmatizing attitudes towards PLWH (mean (SD))	11.79 (20.90)	35.71 (12.37)	0.052**
Support			
Received Social Support (mean (SD)) (range 0-3)	1.87 (0.69)	2.25 (0.80)	0.340
Provided Social Support (mean (SD)) (range 0-3)	2.08 (0.69)	2.20 (0.89)	0.776
Received financial support (mean (SD))	49.40 (27.99)	79.37 (11.00)	0.069
Provided financial support (mean (SD))	60.50 (31.25)	59.92 (44.68)	0.975

Note:*p<0.1; **p<0.05; ***p<0.01

This table includes data from the 97 participants who had refill timing adherence data at month six. Reports were dichotomized as "good refill timing" if women came for their refills within two days of their scheduled appointment time (n=94) and "late refill timing" if participants came more than two days late (n=3).

Table 6. Multiple logistic regression models assessing the impact of individual and network-level social support and stigma variables on viral suppression (< 30 mL/copies) among Kenyan women living with HIV

	Support		Stigma	
	Individual β (SE)	Network β (SE)	Individual β (SE)	Network β (SE)
Age	0.061**	0.060**	0.067**	0.060**
	(0.026)	(0.026)	(0.027)	(0.026)
Finances	0.12	0.105	0.134	0.104
	(0.16)	(0.158)	(0.161)	(0.158)
Sex Worker	-0.48	(0.511	-0.347	-0.529
	(0.655)	(0.650)	(0.668)	(0.649)
Number	0.009	0.005	0.006	0.005
	(0.057)	(0.056)	(0.055)	(0.056)
Intervention Condition	0.303	0.290	0.343	0.309
	(0.440)	(0.441)	(0.444)	(0.441)
Support – Individual	-0.096			
	(0.216			
Support - Network		0.068		
		(0.212)		
Stigma - Individual			0.27	
			(0.224)	
Stigma - Network				-0.059
				(0.215)
SSS				
Constant	-1.519	-1.384	-1.815	-1.395
	(1.204)	(1.182)	(1.242)	(1.179)
Observations	106	106	106	106
Log Likelihood	-64.9	-64.95	-64.26	-64.97
AIC	143.8	143.9	142.5	143.9

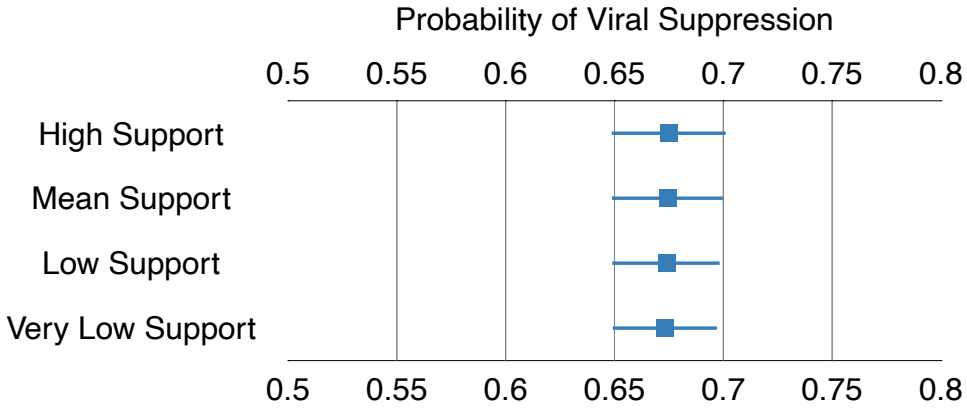
Note:*p<0.1; **p<0.05; ***p<0.01

Table 7. Multiple logistic regression models assessing the impact of individual and network-level social support and stigma variables on ART adherence (VAS) at month six among Kenyan women living with HIV

	Support		Stigma	
	Individual β (SE)	Network β (SE)	Individual β (SE)	Network β (SE)
Age	-0.014	-0.01	-0.012	-0.014
	(0.032)	(0.032)	(0.032)	(0.032)
Finances	-0.222	-0.188	-0.196	-0.206
	(0.205)	(0.207)	(0.207)	(0.208)
Sex Worker	-0.352	-0.352	-0.24	-0.271
	(0.771)	(0.749)	(0.751)	(0.753)
Number of Alters	-0.081	-0.07	-0.063	-0.066
	(0.076)	(0.072)	(0.072)	(0.073)
Intervention Condition	0.611	0.643	0.57	0.588
	(0.598)	(0.595)	(0.593)	(0.593)
Support - Individual	0.193			
	(0.312)			
Support - Network		-0.265		
		(0.307)		
Stigma - Individual			0.156	
			(0.281)	
Stigma - Network				-0.031
				(0.285)
SSS				
Constant	3.218*	2.943*	2.843*	2.985*
	(1.676)	(1.629)	(1.643)	(1.617)
Observations	98	98	98	98
Log Likelihood	-42.032	-41.83	-42.066	-42.216
AIC	98.064	97.66	98.132	98.432

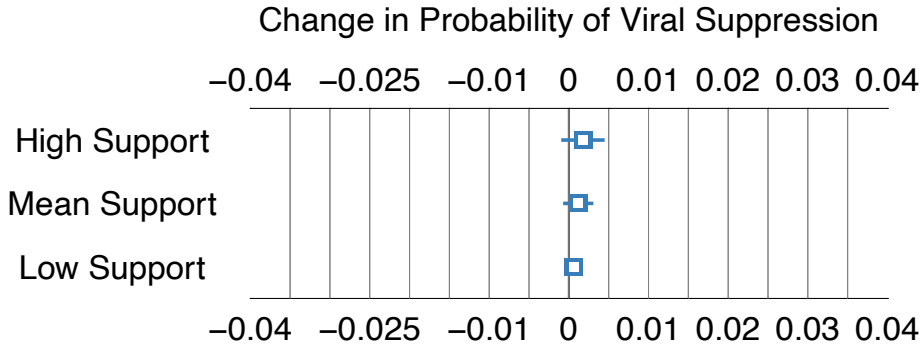
Note: *p<0.1; **p<0.05; ***p<0.01

Figure 1. Expected probability of suppression given different simulations of support within the imputed dataset



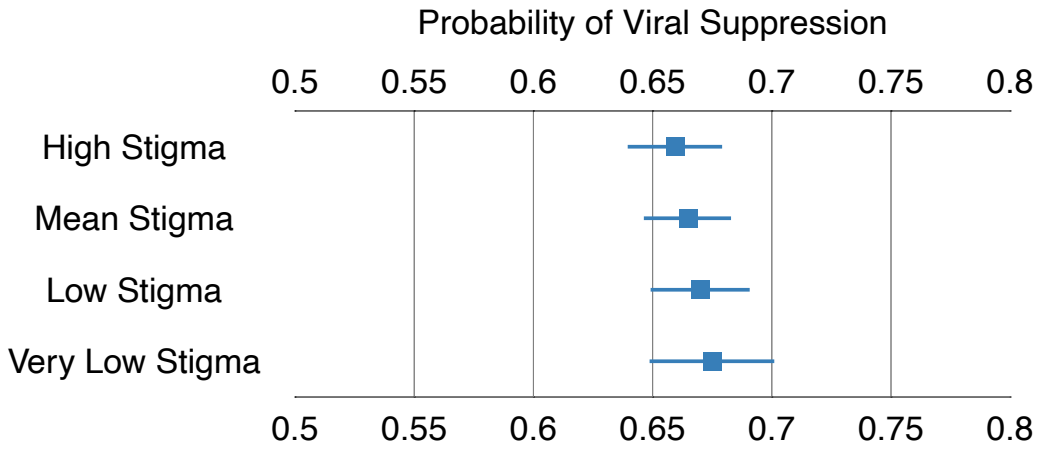
This figure simulates the change in probability by adding an additional supportive alter.

Figure 2. Change in probability of viral suppression with each addition of a supportive alter, relative to having no fewer supportive alters, within the imputed dataset



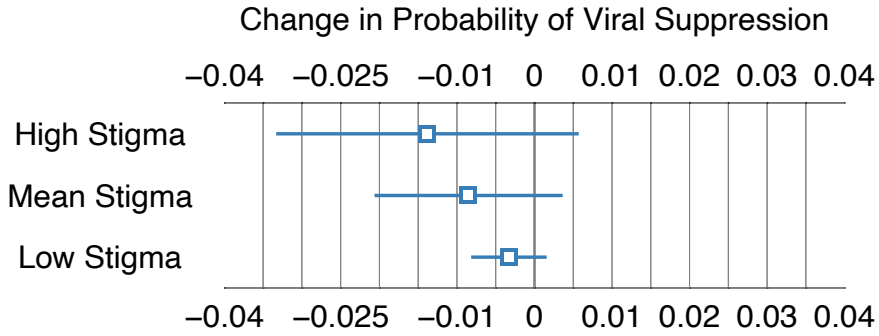
This figure shows the change in probability of suppression based on the changing levels of support. In this simulation, stigma is held consistently low while supportive alters are added. Relative to the comparison condition of having no stigmatizing alters, the "low support" simulation highlights the change in probability of viral suppression between having 10 supportive alters and having 9 supportive alters. The "mean support" simulation compares the change in probability of viral suppression of having 11 supportive alters compared to 9 supportive alters. And finally, the "high support" highlights the change in probability of viral suppression between having all 12 supportive alters compared to 9 supportive alters.

Figure 3. Expected probability of suppression given different simulations of support within the imputed dataset



This figure simulates the change in probability by adding an additional stigmatizing alter.

Figure 4. Change in probability of viral suppression with each addition of a stigmatizing alter, relative to having no stigmatizing alters, within the imputed dataset



This figure shows the change in probability of suppression based on the changing levels of stigma. In this simulation, support is held consistently high while stigmatizing alters are added. Relative to the comparison condition of having no stigmatizing alters, the "low stigma" simulation highlights the change in probability of viral suppression between having no stigmatizing alters and having one stigmatizing alter. The "mean stigma" simulation compares the change in probability of viral suppression of having two stigmatizing alters compared to no stigmatizing alters. And finally, the "high suppression" simulation highlights the change in probability of viral suppression between having three stigmatizing alters compared to no stigmatizing alters.

Chapter V.

Conclusion

This dissertation focused on improving HIV treatment for women living with HIV who engage in sex work in Mombasa, Kenya. As a key population bearing a disproportionate burden of HIV, it is clear our current HIV treatment strategies are not sufficient to meet their needs. Identifying novel intervention strategies to improve rates of ART adherence and viral suppression and using innovative measurement strategies to better understand barriers to treatment are both necessary and required.

My dissertation sought to strengthen both the services provided to women living with HIV and the understanding of factors influencing barriers and facilitators of ART adherence and viral suppression. Chapter I described the process of integrating theory, empirical research, and feedback from FGDs to develop the IMB-informed mHealth intervention, entitled *Motivation Matters!*, to improve viral suppression. Subsequently, we pilot tested *Motivation Matters!* in a randomized controlled trial. Chapter II, then, presented data on the main effect of the intervention on viral suppression, and explored feasibility and acceptability indicators and participant feedback regarding the intervention. While we lacked power to find significant effects, non-significant trends suggested that *Motivation Matters!* may improve viral suppression and ART adherence. High rates of participation and favorable participant feedback support subsequent intervention testing in a larger multi-site trial. Finally, Chapter III sought to understand the relative effect of social support and stigma on ART adherence and viral suppression through individual and network-level measures. Contrary to our hypotheses, social support and stigma did not significantly influence ART adherence or viral suppression. In an effort to explain this surprising finding, we used egocentric network data to unpack the relative impact of social support and stigma at the alter level and found that stigma seemed to be more salient than social support when predicting viral suppression.

Interventions are often most effective for certain subsets of the population, but little research adequately addresses these disparate intervention effects. In the case of HIV, social context is central. A more in-depth understanding of the social context may provide important information for identifying populations most likely to benefit from existing interventions, and designing and tailoring interventions for maximal effectiveness.

A growing body of literature suggests that social network analysis has the potential to provide important information concerning the impact of stigma and social support on health outcomes. While this dissertation begins to address some of these concerns, several significant holes in the literature remain; addressing these could improve our understanding of factors influencing ART adherence and viral suppression:

First, there is limited social network research examining predictors and correlates of ART adherence and viral suppression. Given the necessity of near-perfect adherence for ART to be effective, understanding factors contributing to ART adherence and viral suppression are crucial to informing the development of effective interventions.

Second, more information is needed about the relative impact of social support and stigma at the network level. As is clear from the social support literature, the availability of social support does not always mean that it is accessed. Likewise, there is increasing evidence that characteristics of both the individual and the alter may influence this relationship. Further research about both stigma and social support on a network level will provide a more nuanced picture of the relationship between social support and stigma, and highlight how they may impact health behavior.

Finally, understanding the relationship between social support and stigma may be especially important in the case of dually stigmatized populations, like PLWH who also engage

in sex work or inject drugs, and who may be more likely to be dependent on support from the same people they perceive as stigmatizing. Prevailing literature suggests that stigma and social support are important factors influencing an individual's propensity to take ART, yet few studies have examined these three factors together at a network level. This dissertation, critically, was the first study to assess social support and stigma among women who engage in sex work at the network level. More research is needed to explore the relationship between these three factors and examine whether the relationships found in this study surface in other populations.

In summary, social network analysis offers an innovative way to examine the contributions of social support and stigma to ART adherence among key populations, like women who engage in sex work in sub-Saharan Africa. Social network modeling is an insightful mechanism and methodology to interpret the experience of stigma, and provides tools for understanding factors that might influence both the development and consequences of HIV-related stigma. In order to develop more effective behavioral interventions for PLWH that address their unique needs, it will be essential to have a richer, more in-depth structural description of how individuals operate as social beings within their specific social network. Such an approach will enable researchers to more effectively combat stigma and to optimally manage HIV in key populations.