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Social Capital and Social Networks Improve HIV Health Outcomes: A Global Perspective

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SoSon Jong

DISSERTATION

Submitted in partial satisfaction of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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in the

GRADUATE DIVISION

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by

SoSon Jong

Dedication

For my families and friends
Special thanks to
SoonJa Inn and WooJin Jong, my parents
Soyeon,
Keunyoung,
Patricia,
And Kyunghoon.

3000 Shiling for two Muzungu on BodaBoda
6000 Shiling for a pot of spiced Uganda coffee
Chilling under Mango tree
Green mango next to green papaya

Seizing the moment, last day in Uganda

By Soson Jong

October 24, 2014

At Café Carper diem, Entebbe, Uganda

Abstract

Social capital is features embedded in social networks, such as social norms and trust.

This dissertation aimed to deepen understanding of the effect of social capital on health outcomes among people living with HIV (PLWH) in the context of global health.

Chapter two scrutinized the complexity of the concept of social capital to find out which aspects of the concepts play a major role in relation to better health outcomes. Then chapter three reviewed application of the concept in clinical practice; a meta-analysis examining efficacy of mobile phone reminders on improving HIV patients' return to care. Chapter four applied social capital theoretical framework for PLWH in a resource limited, clinical setting and to inform future studies.

Chapter two identified the importance of social connections over other aspects of social capital such as community participation, trust, and feeling of safety. The findings suggest that social networks to promote health related quality of life among PLWH needed to be strengthened. Also, this study found a mediating effect of engagement with health care providers between social capital and health related quality of life.

Chapter three included nine studies into the systematic meta-analysis and found that PLWH who received mobile phone reminders for their follow-up appointments were two times more likely to return to the care than those who did not received the reminders; however, this estimate was not statistically significant (pooled odd ratio (OR)=2.04, 95% confidence interval (CI): 0.97-4.27). Sensitivity analysis drew stronger evidence of the efficacy of mobile phone reminders on retention in care based on five randomized controlled studies (OR=2.04, 95% CI: 1.11-3.74).

Chapter four found that social capital was an independent predictor of higher quality of life based on a cross-sectional study of 163 PLWH in Dar es Salaam,

Tanzania. Women were more likely to have less social capital and report lower quality of life compared to men.

This dissertation contributed to socio-behavioral and nursing research by elucidating the importance of social capital and suggesting clinical implications of social capital to improve health outcomes among PLWH in a global perspective.

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1 Chapter One: Introduction

1.1 HIV and retention to care

The World Health Organization (WHO) estimates that worldwide HIV prevalence for adults between 18 to 49 years old is 0.8% (WHO, 2014). In the United States, there are about 1,106,400 people living with HIV (PLWH) and only about 79% of them are aware of their status (Gardner, McLees, Steiner, Del Rio, & Burman, 2011). As an epicenter of HIV, sub-Saharan countries account for over 70% of HIV prevalence and one in every 20 adults is living with HIV in sub-Saharan Africa. Despites cooperative global efforts to offer large scale access to highly active antiretroviral therapy (HAART), HIV/AIDS remains a major cause of death in many developing countries, particularly in sub-Saharan Africa (WHO, 2014).

Patient retention to care is a central challenge in the provision of health care not only because of patient care costs and constraints on health care resources but also because of poor health outcomes associated with missed or lost visits. Missed visits are a significant predictor of progression of HIV (Berg et al., 2005). Obviously, people who do not return for periodic appointments are eventually lost to follow-up (LTFU).

LTFU is used as a binary outcome to assess patient retention in HIV care. LTFU has been defined as 'patient does not present to medical appointment within 180 days from the last clinic visit based on multi-center data on HIV patients (111 health facilities from 19 countries) (Chi et al., 2011). The rate of LTFU in treatment programs varies widely, ranging from 5 to 40 percent within 6 months of HAART initiation in resource-limited settings (Losina et al., 2009).

The United President's Emergency Plan for AIDS Relief (PEPFAR) has provided life-saving HIV treatment to 7.7 million PLWH to 65 countries and 20 countries are in Africa (PEPFAR, 2015). In PEPFAR countries, up to two-thirds of people diagnosed with HIV are lost to follow-up before starting HIV treatment (Rosen & Fox, 2011). In the United States, among those who are aware of their status, 25 to 44 percent of PLWH who initially participate in HIV treatment programs are subsequently LTFU. Thus, less than 50 percent of PLWH are actively engaged into HIV care (Gardner et al., 2011).

1.2 Social determinants of HIV care

HIV is a disease precipitated by, and leading to, social, economic and health disparities. Social determinants of health—"circumstances where people are born, grow up, live, and the system in place to deal with illness" (World Health Organization, 2007)—play an important role in HIV prevention and treatment. Internationally, young women continue to be the most vulnerable to HIV. In the United States, the incidence of HIV is increasing among young women, people of color and men who have sex with men (MSM). Gender, race, and social class appear to be critical factors in the acquisition of HIV (Centers for Disease Control and Prevention, 2011). These factors are also associated with LTFU in HIV care. Insurance status, age, gender, and substance use were significant predictors for LTFU (Car, Gurol-Urganci, de Jongh, Vodopivec-Jamsek, & Atun, 2012; Perron et al., 2010). Social and interpersonal factors such as social cohesion, networks and capital are important social determinants of health and understanding them is critical for extended social context (CDC, 2014; National Institutes of Health, 2001).

1.3 Social capital on HIV health outcomes

Social capital is defined as "features and resources--social norm and trust, for example, embedded in a social structure which are accessed and/or mobilized in purposive action" (Lin, 1999; Putnam, 2001). People with high social capital have better health outcomes including higher self-rated health status and lower mortality (Kawachi, Kennedy, & Glass, 1999). Those endowed with social capital experience less barriers accessing health care and tend to build more trusting relationships with health care providers (Perry, Williams, Wallerstein, & Waitzkin, 2008; Torres, Erwin, Trevino, & Jandorf, 2013).

The positive effect of social capital has been consistent among PLWH. Social capital improves HIV outcomes through reduction in stigmatization in a given community. A strong relationship between social capital and perceived HIV stigma has been identified. PLWH living in a community with high social capital experienced less HIV stigma (Chiu et al., 2008; Sivaram et al., 2009). People with perceived community trust and safety, in other words, high social capital, are less likely to have stigmatizing behaviors toward HIV-infected community members. Another pathway of social capital on positive HIV health outcomes is through improving perceptions of safety and connections among community members (Ziersch, Baum, Macdougall, & Putland, 2005). Women with high social capital, community participation and memberships, had lower HIV incidence over time and were more likely to adapt safer sexual behavior in Zimbabwe (Gregson et al., 2011).

1.4 Technology promotes social capital

Due to technical innovation and universal and nearly ubiquitous access to internet, there has been increased interest in and usage of social networking applications. In addition, mobile phone technology promotes the flow of information, strengthens ties among

people, and enhances participation in civil society, all of which are core aspects of social capital (Lin, 1999; Ling, 2008; Putnam, 2001). Social network is a structure where social capital flows and amplifies. Therefore, there is little doubt that the currency of social networks--easily accessible information and networking capability over mobile networks--is a form of social capital. In addition, mobile technology can also offer great potential in promoting communication and education between health providers and their patients (Lin, 1999).

1.5 Research questions

The majority of research done on social capital and health is limited to observational studies. With recent technological innovations and efforts to improve comprehensive approaches toward health intervention, research studies have looked at interventions using mobile technology, ranging from reminders to take medication, increased physical activity, and follow up with future appointments and to monitor bio-markers (Car et al., 2012; Coomes et al., 2012; Finitsis, Pellowski, & Johnson, 2014). Periodic mobile text messages asking PLWA's welfare—How are you? —, followed by phone calls by health care providers if PLWA do not respond for 2 days or respond as 'I'm not well', significantly improved HIV medication adherence in Kenya (Lester et al., 2010). Despite growing research in this area, interventions using mobile technologies are still in early stages and are not fully utilizing social networking capabilities (Coomes et al., 2012). As far as reminders are concerned, for example, shifting from postcard or mail to mobile phone text messages reminders did not have greater impacts on targeted outcomes follow-up appointments. Despites the usefulness of theory to guide comprehensive research design, relevant data collection and analysis, studies often underestimate how

theory can increase understanding of why an effect is occurring or not (Reeves, Kuper, & Hodges, 2008).

Given these gaps in the literature, this dissertation attempts to answer the following questions, 'Does high social capital improve health outcomes for PLWH?' and 'How can we design more effective and sustainable interventions to improve HIV health outcomes, with a focus on increasing retention to HIV care?'

1.6 Purpose

The purpose of this dissertation is to evaluate the concept of social capital in social networks among PLWH and to examine its application in relation to their HIV health outcomes. This dissertation aims to improve clinicians and researchers' understanding on importance of PLWH's social capital and networks to attain better health.

This dissertation is organized as follows. First, the concept of social capital was examined in relation to health outcomes among PLWH. Second, a systematic review of social capital and its' relationship to technology adoption to improve health care delivery in resource-limited settings was conducted. Lastly, a pilot study was conducted to examine the association social capital and PLWH's health outcomes in resource-limited settings.

The first chapter examines the relationships between social capital and HIV patients' health related quality of life mediated by relationships with primary health care providers. The secondary data analysis was drawn from HIV network study 5, which enrolled more than 2000 HIV patients from U.S.A., Canada, Namibia, Puerto Rico, and Thailand. Results from this study, based on study participants from United States (n=1673), found a positive effect of social capital on quality of life, which was mediated

by patients' relationships with their health care providers. The study found that building a trusting relationship and sharing information and knowledge within social networks are primary elements of social capital. Findings from this study suggest that encouraging and promoting trusting relationships with health care providers is a primary component of better management of HIV.

The second chapter systematically reviews the current evidence of the effectiveness of text message reminders on retention to care among people with, or at high risk of, HIV. Nine studies (5 randomized controlled and 4 before and after controlled studies) from 7 countries included 3,004 participants. The most commonly represented participant profile in the sample was a 34 year-old female in Africa. HIV clinics sent automated text message reminders to clients prior to follow-up appointments for follow-up appointments. People who received text message reminders were twice more likely to return to the care compared to people who did not receive the messages (pooled OR=2.04, 95% CI: 0.97-4.27). Sub-group analysis of six studies from Africa revealed that the intervention had significant effect on their return to care (pooled OR=2.92, 95% CI: 1.13-7.53).

The last chapter presents the results of a pilot study conducted from six HIV clinics in Dar es Salaam, Tanzania in summer of 2015. The study aims to understand whether social capital can improve HIV patients' health outcomes—specifically, early diagnosis of HIV, and starting HIV treatment on time, retention to care, and HIV disclosure. The study assessed patients' health status at the time of engagement to care, HIV quality of life and retention to care. The study reinforced independent and important role of social capital predicting better health outcomes among the study

participants and also highlighted the role of poverty and gender inequality in social capital.

Each chapter is closely related to each other. The path of social capital to one of HIV health outcomes, self-reported quality of life in relation to health, was identified. Social capital, the currency of social networks, was mediated by relationships with health care providers to lead better quality of life among PLWH. Then, the meta-analysis examined clinical evidence about whether text-message reminders initiated by health care systems can lead to higher re-attendance rate. Finally, the pilot study builds upon the previous two chapters, and aims to study the associations between social capital and HIV health outcomes among PLWH in Tanzania.

References

- Berg, M. B., Safren, S. A., Mimiaga, M. J., Grasso, C., Boswell, S., & Mayer, K. H. (2005). Nonadherence to medical appointments is associated with increased plasma HIV RNA and decreased CD4 cell counts in a community-based HIV primary care clinic. *AIDS Care*, *17*(7), 902-907. doi:W74171324K2312M1 [pii]
- Car, J., Gurol-Urganci, I., de Jongh, T., Vodopivec-Jamsek, V., & Atun, R. (2012).

 Mobile phone messaging reminders for attendance at healthcare appointments. *The Cochrane Database of Systematic Reviews, 7*, CD007458.

 doi:10.1002/14651858.CD007458.pub2; 10.1002/14651858.CD007458.pub2
- CDC. (2014). HIV among women. Retrieved from http://www.cdc.gov/hiv/risk/gender/women/facts/index.html
- Centers for Disease Control and Prevention. (2011). *HIV surveillance report*. (No. vol.23.).
- Chi, B. H., Yiannoutsos, C. T., Westfall, A. O., Newman, J. E., Zhou, J., Cesar, C., . . . International Epidemiologic Databases to Evaluate AIDS Collaboration. (2011).

 Universal definition of loss to follow-up in HIV treatment programs: A statistical analysis of 111 facilities in africa, asia, and latin america. *PLoS Medicine*, 8(10), e1001111. doi:10.1371/journal.pmed.1001111 [doi]
- Chiu, J., Grobbelaar, J., Sikkema, K., Vandormoel, A., Bomela, N., & Kershaw, T. (2008). HIV-related stigma and social capital in south africa. *AIDS Education and*

- Prevention: Official Publication of the International Society for AIDS Education, 20(6), 519-530. doi:10.1521/aeap.2008.20.6.519; 10.1521/aeap.2008.20.6.519
- Coomes, C. M., Lewis, M. A., Uhrig, J. D., Furberg, R. D., Harris, J. L., & Bann, C. M. (2012). Beyond reminders: A conceptual framework for using short message service to promote prevention and improve healthcare quality and clinical outcomes for people living with HIV. AIDS Care, 24(3), 348-357. doi:10.1080/09540121.2011.608421 [doi]
- 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; 10.1371/journal.pone.0088166
- Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, *52*(6), 793-800.

 doi:10.1093/cid/ciq243 [doi]
- Gregson, S., Mushati, P., Grusin, H., Nhamo, M., Schumacher, C., Skovdal, M., . . .

 Campbell, C. (2011). Social capital and women's reduced vulnerability to HIV infection in rural zimbabwe. *Population and Development Review*, *37*(2), 333-359.
- Kawachi, I., Kennedy, B. P., & Glass, R. (1999). Social capital and self-rated health: A contextual analysis. *American Journal of Public Health*, 89(8), 1187-1193.

- 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. *Lancet,* 376(9755), 1838-1845. doi:10.1016/S0140-6736(10)61997-6
- Lin, N. (1999). Building a network theory of social capital. Connections, 22(1), 28-51.
- Ling, R. S. (2008). *New tech,new ties: How mobile communication is reshaping social cohesion*. Cambridge, Massachusetts: The MIT Press.
- Losina, E., Toure, H., Uhler, L. M., Anglaret, X., Paltiel, A. D., Balestre, E., . . . CEPAC International investigators. (2009). Cost-effectiveness of preventing loss to follow-up in HIV treatment programs: A cote d'ivoire appraisal. *PLoS Medicine*, *6*(10), e1000173. doi:10.1371/journal.pmed.1000173 [doi]
- National Institutes of Health. (2001). Toward higher levels of analysis: Progress and promise in research on social and cultural dimensions of health. executive summary. (No. 21-5020).
- Perron, N. J., Dao, M. D., Kossovsky, M. P., Miserez, V., Chuard, C., Calmy, A., & Gaspoz, J. M. (2010). Reduction of missed appointments at an urban primary care clinic: A randomised controlled study. *BMC Family Practice, 11*, 79-2296-11-79. doi:10.1186/1471-2296-11-79; 10.1186/1471-2296-11-79

- Perry, M., Williams, R. L., Wallerstein, N., & Waitzkin, H. (2008). Social capital and health care experiences among low-income individuals. *American Journal of Public Health*, *98*(2), 330-336. doi:10.2105/AJPH.2006.086306 [doi]
- Putnam, R. D. (2001). Social capital: Measurement and consequences. *Isuma:*Canadian Journal of Policy Research, 2
- Reeves, S., Kuper, A., & Hodges, B. D. (2008). Qualitative research methodologies: Ethnography. *BMJ (Clinical Research Ed.)*, 337, a1020. doi:10.1136/bmj.a1020
- Rosen, S., & Fox, M. P. (2011). Retention in HIV care between testing and treatment in sub-saharan africa: A systematic review. *PLoS Medicine*, *8*(7), e1001056. doi:10.1371/journal.pmed.1001056 [doi]
- Sivaram, S., Zelaya, C., Srikrishnan, A. K., Latkin, C., Go, V. F., Solomon, S., & Celentano, D. (2009). Associations between social capital and HIV stigma in chennai, india: Considerations for prevention intervention design. *AIDS Education and Prevention: Official Publication of the International Society for AIDS Education*, 21(3), 233-250. doi:10.1521/aeap.2009.21.3.233; 10.1521/aeap.2009.21.3.233
- Torres, E., Erwin, D. O., Trevino, M., & Jandorf, L. (2013). Understanding factors influencing latina women's screening behavior: A qualitative approach. *Health Education Research*, *28*(5), 772-783. doi:10.1093/her/cys106 [doi]
- WHO. (2014). Global health observatory (GHO), HIV/AIDS: Global situation and trends.

 (No. 2014). Switzerland, Geneva: World Health Organization (WHO).

- World Health Organization. (2007). WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.
- Ziersch, A. M., Baum, F. E., Macdougall, C., & Putland, C. (2005). Neighbourhood life and social capital: The implications for health. *Social Science & Medicine (1982),* 60(1), 71-86. doi:10.1016/j.socscimed.2004.04.027

2 Chapter Two: Path-analysis: Engagement with health care providers as a mediator between social capital and quality of life among people living with HIV in the States

2.1 Introduction

Social capital is defined as 'features of social organizations such as networks, norms, and as trust that facilitate coordination and cooperation for mutual benefit' (Putnam, 2001). Harpham and colleagues (2002) emphasizes its aspects of social networks and defines social capital as 'the degree of connectedness and the quality and quantity of social relations in a given population' (Harpham, Grant, & Thomas, 2002). French sociologist and philosopher Pierre Bourdieu referred social capital as a "collective of actual or potential resources linked and shared by institutionalized relationships, so to speak, group membership' (Bourdieu, 1986). Bourdieu regarded social capital as instrumental so the group membership is not automatically given and networking is a form of investment by the individual or the collective thriving for resources (Bourdieu, 1986).

Social capital remains a complex concept and renowned theorists hold different perspectives on social capital. Despite differences in the definitions of social capital, there are major attributes that penetrate the concept. Social capital is both a tangible and an intangible resource from the individual to the community level. The production and use of social capital occurs between and among people (relationships) who are pursuing certain shared goals. The use of social capital can help people to take actions toward their goals.

Social capital highlights the importance of social relationships necessary to attain health. Therefore, understanding social capital is critical for understanding the influences of social and cultural systems among families, and in neighborhoods and communities (National Institutes of Health, 2001). The positive effects of social capital on health have been well studied. People with high social capital have better health outcomes including higher self-rated health status and lower mortality (Kawachi, Kennedy, & Glass, 1999). A review of the literature found that people residing in more walkable neighborhoods are more likely to have lower rates of obesity and depression, increased physical activity, and less alcohol abuse (Renalds, Smith, & Hale, 2010). Additionally, the impact of neighborhood factors on birth outcomes, such as low birth weight, is well documented (Metcalfe, Lail, Ghali, & Sauve, 2011).

Difficulty of measuring social capital inherits from the complexity of the concept (Derose & Varda, 2009; Harpham, Grant, & Thomas, 2002). Accordingly, developing interventions that target social capital is even more challenging. Despite these challenges, measuring and strengthening social capital is crucial, because social interconnectivity and support that arises from this connectedness are important influences on human health behaviors.

2.1.1 Social Capital and HIV Outcomes

HIV is a disease fraught with disparities (Centers for Disease Control and Prevention, 2011). Social capital, an important determinant of health, may play a role in HIV prevention and treatment. An ecologic study from Zimbabwe showed that women with high social engagement and capital had lower HIV incidence over time and were more likely to adopt safer sexual behaviors (Gregson et al., 2011). Social capital can improve

HIV outcomes through a reduction in stigmatization. Community trust and safety are two of the most important attributes of social capital. PLWH with high social capital are less likely to experience stigma and people with higher social capital are less likely to engage in stigmatizing behavior toward HIV-infected community members (Kreuter. M & Lezin. N, 2002). This is particularly important in that it suggests building social capital in communities leads to a change in social norms (Chi et al., 2009).

Stigma against PLWH is a known barrier to accessing HIV testing and care and perceived stigma negatively affects the quality of life of PLWH (Holzemer et al., 2007). A study from India explored two domains of social capital, group membership/network and collective action, and found an association between social capital and stigma, such as reduced fear of HIV transmission and lower levels of feelings of shame (Sivaram et al., 2009). High norms of reciprocity, higher levels of collective action, and perception of safety have been found to be related to lower HIV stigma (Chi et al., 2009; Sivaram et al., 2009).

2.1.2 Relationship with Health Care Providers, Social Capital and Quality of Life

Chronic health conditions like HIV infection require long term health care services.

Therefore relationships with health care providers (HCP) play an important role in health outcomes. Studies have shown associations between social capital and engagement with HCP, leading to better health outcomes. Torres et al. found that trust and better communication with HCP predicted better health-related behaviors, such as breast cancer screening, among low-income Latinas. Women with higher community engagement also showed similar positive health behaviors (Torres, Erwin, Trevino, &

Jandorf, 2013). Higher community social capital independently predicted the level at which patients trusted their physicians (Ahern & Hendryx, 2003). Also, social capital lowered barriers to health care access and promoted higher trust in HCP and staff (Derose & Varda, 2009). Although availability of a HCP may vary depending on participants' resources, it is clear that the ability to engage with one's HCP and build trusting relationship is driven by a person's social capital.

A meta-analysis of 13 randomized controlled trials found a small but significant effect of patient-HCP relationship both on subjective pain, Quality of Life (QoL), psychosocial aspects and objective (blood pressure, weight loss) health outcomes (effect size (d)=0.11, p=0.02) (Kelley, Kraft-Todd, Schapira, Kossowsky, & Riess, 2014). In addition, a high quality patient and HCP relationship, defined as patients' perception of their provider knowing them 'as a person', was independently associated with HIV health outcomes measured by adherence to antiretroviral therapy for HIV and undetectable HIV RNA in serum (Beach, Keruly, & Moore, 2006). Considering those relationships among social capital, trusting relationships with HCP, and health outcomes, patients' engagement with their HCP may mediate the path between social capital and health outcomes.

2.1.3 Study objectives

The aim of this study is to measure the effect of social capital on HIV health outcomes. Considering its multi-dimensional attributes, we examined major domains of social capital leading to positive HIV health outcomes measured by health-related QoL. Our primary hypothesis is that people with high social capital are able to manage their HIV disease better, leading to improved QoL. We hypothesized that the relationship

between social capital and QoL is mediated by engagement with health care providers. Using path analysis, we examined the independent effect of social capital on QoL, as well as the mediating effect of patient engagement with HCP. Certain dimensions of social capital, such as 'community participation' and 'feeling of safety in community', may explain the majority of the variance in the relationship between social capital and QoL. Therefore our secondary hypothesis is that certain dimensions of social capital explain the mediation between social capital and QoL.

2.2 Methods

2.2.1 Materials and methods

This is a secondary analysis of the International Nursing HIV Network for HIV/AIDS Research study described previously (Webel et al., 2012). This study was a multi-site, international, cross-sectional study conducted between August 2009 and December 2010 with 2,182 persons with HIV/AIDS in 16 research sites from 6 countries (Canada, China, Namibia, Thailand, and the United States). For the present analysis, the analytical sample included U.S. respondents (n=1,673) from 11 research sites. Participants were mostly male (71.2%), and had a median age of 45 years. Stata 13.1 was used for statistical analysis.

2.2.2 Measures

Social Capital

The Measuring Social Capital (MSC) instrument was administered to measure individual social capital (Onyx & Bullen, 2000). MSC has 36 items measuring 8 dimensions of social capital—participation in the local community (7 items), social agency (7 items), feelings of trust and safety (5 items), neighborhood connections (5 items), family and

friend connections (3 items), tolerance of diversity (2 items), value of life (2 items) and work connection (3 items). Each item employs a four-point Likert-type scale from 1 (no, not much or no, not at all) to 4 (yes, definitely or yes, frequently). Higher scores represent higher levels of social capital among individuals. The instrument is valid and reliable in measuring social capital with a Cronbach's alpha coefficient of 0.84. The average of the total score is used to interpret the level of social capital, with 1 equal to very low social capital and 4 equal to very high social capital (Onyx & Bullen, 2000). The score can be analyzed continuously or categorically. A dichotomous cutoff point of 2.5 can be used to categorize social capital into low versus high. We excluded three items from work connection due to low level of employment among the sample.

Quality of Life

SF-12 is a shorter version of SF-36, which is widely used for assessing quality of life in relation to health status. SF-12 includes physical and mental health components based common sub-domains—general health perceptions, bodily pain, physical functioning, social functioning, mental health and energy/vitality. The composite scores derived from twelve questions range from 0 to 100, continuously; higher scores indicate better quality of life in relation to health status. SF-12 is a well-validated and reliable measure based on both U.S. population and internationally (Chronbach's α =0.86 and 0.76, physical and mental, respectively) (Ion et al., 2011; Revicki & Kaplan, 1993).

Engagement with HCP

The scale evaluating participants' interaction with their HCP is comprised of 13 items.

Using a 4 point Likert scale (1=always true and 4=never), a lower score indicates

greater engagement with HCP (Bakken et al., 2000). The composite score is measured

continuously and ranges 13-52. This instrument has one factor, engagement with HCP (Eigen-value of 6.8 and 66.5% of variance explained), and high reliability (Chronbach's α =0.96) (Bakken et al., 2000). Because data had a non-normal distribution, the score was Log₁₀ transformed (Skewness=1.93).

2.2.3 Analysis

Factor Analysis

Factor analysis is a statistical technique for determining construct-related evidence. Psychometric tests often employ multiple items to capture multi-dimensional characteristics of a concept such as social capital. Factor analysis assists in identifying the major constructs that make up the concept (structure of the concept) by examining relationships between items as well as between items and the construct. When the items cluster together, the factor analysis can provide strong evidence of the internal consistency, reliability and construct validity (Munro, 2005b).

Exploratory factor analysis (EFA) is often used to develop an instrument in order to reduce the number of items to produce a parsimonious measure, without losing construct validity. However, EFA requires several strict assumptions: (a) factors cannot be correlated to each other, (b) all factors must directly load on all items, (c) item measurement error should not be correlated, and (d) measurement errors should affect all items equally. These unrealistic assumptions do not apply to confirmatory factor analysis (CFA), allowing more flexibility of psychometric property analysis. Instead, CFA allows theory to guide the process of checking assumptions, as long as it is theoretically appropriate. Another reason why CFA is preferable over EFA to assess the construct

validity of a tool, is that CFA can also assess the configuration of factor structure for the hypothesized model (or theoretical model) and any measurement error (Acock, 2013).

We first conducted EFA using the total score of social capital to examine underlying factors among the U.S. sample. Then we undertook oblique rotation of the data because oblique rotation assumes that factors may correlate to each other and, in particular, important factors do correlate in practice (Munro, 2005b). EFA with oblique rotation suggested three factors that should be retained, based on Eigenvalues greater than 1. Scree plots were also assessed.

During CFA process, we removed three items from the factors based on rotated factor loadings for a better fit of the factor structure. The cut-off for factor loading was greater than 0.30. If loading produced more than one factor, we allocated items to factors with higher loading (Acock, 2013).

We treated three identified factors as latent variables for dimensions of social capital. We calculated a sub-scale score for each factor with error variance specified using the reliabilities of the scales (See Joreskog and Sorbom, as cited in Rustoen and Cooper, 2010; p529-530, Acock, 2015).

Path analysis

We used path analysis to examine the direct and indirect effect (the mediating effect of HCP) of social capital on QoL, using maximum likelihood with missing values. Several parameters were used to evaluate model fit—Chi-square (χ^2) goodness of fit, Root Mean Square Error of Approximation (RMSEA), and Comparative Fit Index (CFI) (Acock 2013). We set p-values > 0.05 for the χ^2 test, < 0.05 for the RMSEA, and > 0.95

(1.0 being a perfect fit) for the CFI to indicate close fit of the model. We reported standardized coefficients to allow comparisons on the same scale between paths.

2.3 Results

2.3.1 Demographic and clinical characteristics of the sample:

This study was based on U.S. study participants (N=1,673). The mean time since initial HIV diagnosis was 14 years (Standard deviation (SD)= 7.5). The majority of the participants were on antiretroviral therapy (88.7%), were male (71.2%) and 45.7% were African American. Approximately, 80% of the sample reported their income was totally inadequate or barely adequate to support their needs (Table 2.1).

2.3.2 Factor analysis of social capital

We identified three underlying factors explaining 83 percent of the variance in the total score of social capital (Table 2.2). Questions such as 'Can you get help from friends when you need it?' or 'Does your local community feel like home?' were in the social connection sub-scale, which measures how close and dense one's social network was within a given community as well as trust and norm in the community. The second factor, community participation, measured how engaged one engaged in and volunteered for community activities using questions like 'Have you ever taken part in a local community project, in the past 3 years?'. The last factor was tolerance towards diversity. Examples of questions are 'Do you think diversity makes life in your area better?, or 'Do you enjoy living among people of different lifestyles?'.

The number of total items measuring social capital was reduced from 31 to 25.

Among the three factors, social connection explained the most of the variance of the social capital (33.3%) followed by community participation (26.1%) and tolerance toward

diversity (24.4%). Cronbach's alpha reliabilities (α) of each factor are presented in Table 2.2. Social connection and community participation had good internal consistency (0.8≤α<0.9) and tolerance toward diversity had acceptable internal consistency (0.7≤α<0.8) (Hulley, Cummings, Browner, Grady, & Newman, 2007; Munro, 2005b).

The social capital score was normally distributed with a mean of 2.67 (standard deviation (SD)=0.54). Social connection was normally distributed with a mean score of 2.69 (SD=0.64). Community participation had relatively low mean score (2.03, SD=0.89) and tolerance toward diversity was high (mean of 3.18, SD=0.67) (Table 2.3). In other words, in this sample, PLWH in the United States reported low participation in community activities while maintaining a high tolerance towards diversity.

While Pearson's correlation coefficients (r) among the variables were all statistically significant, only overall social capital and social connection had moderate correlations to QoL ($|0.3| \le r < |0.5|$) (Table 2.3) (Hulley, Cummings, Browner, Grady, & Newman, 2007; Munro, 2005b). Social connection, community participation, and tolerance towards diversity were all highly correlated to each other ($|0.5| \le r < |1.0|$).

2.3.3 Path analysis

We tested our primary hypotheses in model 1. Social capital was significantly associated with QoL and explained 14% of variance of QoL while engagement with HCP explained 3%. About 11% of positive effect of social capital on QoL was mediated by engagement with HCP (p<0.05)(figure 2.1). This model explained 89% of the variance in QoL, however did not have a good fit (χ^2 =0, RMSEA=0.495, CFI=0).

In order to improve the model fit and to test our secondary hypothesis, we examined the effect of three factors of social capital (Social connection, community

participation, and tolerance towards diversity) and QoL in model 2 (Figure 2.2). Model 2 explains 99% of the total variance with very good fit (RMSEA=0, CFI=1) and tested the mediation between social capital and QoL. Social connection had a significant and substantial association both with QoL (std. beta=0.49) and engagement with HCP (std. beta=-0.14), demonstrating that PLWH who have good social connections were more like to engage with their HCP and to report better QoL. This positive effect of social connection on improved QoL was mediated by engagement with HCP at 4.7%.

Tolerance toward diversity did not present any significant direct association with QoL (std. beta=-0.04) while the standardized estimate of the effect on engagement with HCP was bigger than social connection (std. beta=-0.19 vs -0.14, respectively). As there was no direct effect of tolerance toward diversity on QoL, the positive effect of tolerance toward diversity on QoL is solely mediated by HCP (Table 2.3).

Conversely, community participation showed a reverse association with other variables in the model. Community participation was minimally correlated with QoL (r=less than 0.01) and engagement with HCP (r=less than 0.02) (Table 2.3). When a simple path model conducted solely with community participation, the association with engagement with HCP was not significant (p=0.47) and the association with QoL was positive and significant (p<0.05). Considering the high correlation between the factors, the reverse association is probably due to multicollinearity (Munro, 2005a).

2.4 Discussion

This study is one of the first studies to examine the association between sub-domains of social capital on health outcomes among PLWH in the United States. We found that social connection, followed by tolerance toward diversity, were the principal domain of

social capital leading to better QoL. Other domains of social capital, such as community participation or feelings of safety, did not have an effect on QoL in this sample. Social connection was the leading factor, and its effect was partially mediated by PLWH's engagement with their HCP.

Study participants reported low participation in community activities while their tolerance toward diversity was high. The effect of tolerance toward diversity on QoL was completely mediated by their engagement with their HCP, which highlights the need for building engaging relationships with HCP. Therefore, health care service should not be limited to mere provision of medical services. Rather, helping PLWH to build strong connections with HCP should be an integral part of comprehensive HIV care.

Community participation, often assessed by asking about memberships in community organizations or groups has been one of the important domains of social capital. For example, Kawachi and colleagues assessed social capital in the United States by using 3 questions regarding civic trust, perception of reciprocity, and community group membership (Kawachi, Kennedy, & Glass, 1999). In our analysis, not only was the community participation rate low, but this factor did not predict any meaningful association with other variables. Our sample was recruited from outpatients and community HIV clinics and included a large portion of socio-economically marginalized participants. Sixty-five percent of the participants experienced depressive symptoms and low self-esteem (Eller et al., 2014), which might explain the low rate of community participation.

The study participants also had low education levels and were low-income. SES, often measured by household income and education level, is known to be an

independent predictor of overall health outcomes (Kawachi, Kennedy, & Glass, 1999) and correlates with social capital, therefore, it is an important variable to examine. Controlling for SES may attenuate the association between social capital and health, but social capital is still an independent and significant predictor of health outcomes (Kawachi, Kennedy, & Glass, 1999; Ziersch, Baum, Macdougall, & Putland, 2005). While the association between social capital and SES has been established, directionality between these two variables is not well understood. Therefore, focusing interventions on building supportive social networks for PLWH, may improve QoL, even among those with low SES.

This study was based on a sub-sample of U.S. participants in a large international study. Webel and colleagues reported on study participants from the larger study, including China, Canada, Namibia, Thailand, and the United States. They found a positive effect of social capital on QoL; five factors of social capital explained 65% of the variance in social capital (Webel et al., 2012). Within the sample from the United States, social connection was the leading domain predicting QoL. Social connection is a rather generic concept measured through 13 questions (table 2.2). Thirteen items of social connection were drawn from neighborhood connections, family and friend connections and feelings of trust and safety, which examines how people are well connected within their supportive social networks(Onyx & Bullen, 2000).

There are several limitations of this study. First, our sample was primarily composed of men with HIV in the United States, many of whom reported feeling marginalized; therefore our results may not be generalizable to other groups, including women with HIV. Second, all the measures are based on self-report. Despite the wide

use and established validity of the SF-12 instrument, adding biologic markers may have increased validity in the study findings about quality of life in relation to HIV disease progression. Third, this study is secondary analysis of a cross-sectional study; therefore, causal inference between variables in the model cannot be ascertained.

One of the features of social capital that differentiates it from other concepts, such as social support and social networks, is the level at which the concept resides. Social capital is distinct in that it is a group-level resource with features shared by members and external to individuals. In contrast, perceived social support and social networks are individual attributes and vary for each individual (Luke & Harris, 2007). Community level factors, such as high social capital, have been linked to individual health and wellbeing. People residing in communities with higher levels of social capital are more likely to report better health independent of the effects of socio-economic status, including income and education (Kawachi, Kennedy, & Glass, 1999). At the neighborhood level, social capital also has an impact on health-based perceptions of safety and connections among neighbors (Ziersch, Baum, Macdougall, & Putland, 2005).

2.5 Conclusion

The association between social capital and QoL among PLWH living in the US suggests that . The relationship was mediated by PLWH's engagement with their HCP.

We found three factors to be associated with social capital in this U.S. sample--community participation, social connection, and tolerance towards diversity. Among these factors, only social connection was significantly associated with higher QoL.

Therefore, PLWH who had supportive and resourceful social networks represented by

families, friends and neighbors reported higher QoL as opposed to PLWH who actively participated in or volunteered for community work.

To clarify and expand the model, other covariates such as medication adherence, stigma or gender should be considered in future studies. Enhancing the relationship between HCP and persons infected with HIV/AIDS would also lead to better health outcomes. Interventions that promote resourceful and supportive social connection among PLWH should be promoted.

Table 2.1. Demographic Characteristics (N= 1673)

Variable						
Age (mean, SD, range)	46.1years (9.3, 18-74)					
Gender (%)						
Male	1181 (71.2)					
Female	435 (26.2)					
Transgender (MTF/FTM)	36 (1.5) (12/24)					
Genderqueer/decline to state	6 (0.4) (5/1)					
Race/Ethnicity (%)						
Black	752 (45.7)					
White (non-Hispanic)	436 (26.5)					
Hispanic	327 (19.9)					
Asian/Pacific Islander	50 (3.0)					
Native American/Indian	35 (2.1)					
Other race	47 (2.9)					
Education (%)						
11 th grade or less	407 (24.6)					
High school or GED	678 (40.9)					
Some college or more	524 (31.6)					
Master's degree or more	48 (2.9)					
Income (%)						
Totally inadequate	408 (24.9)					
Barely adequate	881 (53.7)					
Enough	351 (21.4)					
Insurance (%)						
Yes	1270 (76.3)					
No	395 (23.7)					
HIV related characteristics						
HIV years since diagnosis (mean, SD)	14.0 (7.5)					
On Antiretroviral (%)	1446 (88.7)					
Knows own CD4 counts (%)						
Yes	1080 (68.6)					
No	494 (31.4)					
CD4 counts by report (n=1098) (mean, SD)	532.1 (464.9)					

Table 2.2. Exploratory Factor Analysis

Factors	Items	Loadings			
	Do you agree that most people can be trusted? Does your area have a reputation for being a safe place? Does your local community feel like home?	0.41 0.47 0.54			
	4. Can you get help from friends when you need it?5. If you were caring for a child and needed to go out for a while, would you ask a neighbor for help?	0.59 0.46			
	6. Have you ever visited a neighbor in the past week?	0.49			
Factor 1. Social	7. When you go shopping in your local area, are you likely to run into friends and acquaintances?	0.50			
connection	8. How many people did you talk to yesterday?	0.52			
	9. Over the weekend do you have lunch/dinner with other people outside your household?	0.43			
	10. Do you feel valued by society?	0.51			
	11. If you were to die tomorrow, would you be satisfied with what your life have meant?	0.50			
	12. In the past week, how many phone conversation have you had with friends?	0.48			
	13. Do you go outside your local community to visit your family?	0.45			
	Eigenvalue Percent Variance explained (%) Cronbach's alpha reliabilities (α)	6.41 33.3 0.81			
	Do you help out a local group as a volunteer?	0.52			
	2. Have you attended a local community event in the past 6 months?	0.59			
Factor 2.	3. Are you on a management committee or organizing committee for any local group or organization?				
Community participation	4. In the past 3 years, have you ever joined a local community action to deal with an emergency?	0.73			
, ,	5. In the past 3 years, have you ever taken part in a local community project or working bee?	0.76			
	6. Have you ever been part of a project to organize a new service in your area?	0.73			
	Eigenvalue	1.85			
	Percent Variance explained (%) Cronbach's alpha reliabilities (α)	26.1 0.83			
	If you disagree with what everyone else agreed on, do you feel free to speak out?	0.57			
Factor 3. Tolerance	2. If you disagree with what everyone else agreed on, are you willing to seek medication?	0.52			
towards diversity	3. Do you think diversity makes life in your area better?	0.66			
diversity	4. Do you enjoy living among people of different lifestyles?	0.66			
	5. If strangers move in neighborhood, would they be accepted?	0.44			
	6. Do agree with the term, helping other help yourself Eigenvalue	0.40 1.02			
	Percent Variance explained (%)	24.4			
	Cronbach's alpha reliabilities (α)	0.73			
	Items removed f				
Non-loading items=3					
	<u> </u>	otal items=31			

Table 2.3. Pearson's r correlation among variables

Variables	Social Capital	Quality of life	Engage- ment with HCP	Community participation	Social connection	Tolerance towards diversity	Mean Score of Variables (SD)
Social Capital	1						2.67 (0.54)
Quality of life	0.323*	1					43.6 (8.11)
Engagement with HCP	-0.250*	-0.162*	1				1.39 (0.60)
Community participation§	0.688*	0.095*	-0.019*	1			2.03(.89)
Social connection§	0.865*	0.383*	-0.180*	0.431*	1		2.69(.64)
Tolerance towards diversity [§]	0.668*	0.218*	-0.207*	0.262*	0.469*	1	3.18(.67)

^{• *} P<0.05

Table 2.4. Standardized effect of Social capital and QoL with medication of HCP

Model 2	Direct effect	Indirect effect	Total effect	Indirect effect of HCP (%)
Community participation→QoL	143*	020*	163*	12.3
Social Connection→QoL	.493*	.023*	.518*	4.7
Tolerance towards diversity→QoL	041	.030*	010	100

^{*}P<0.05

 [§] Factor variables of 'social capital'

Figure 2.1 Model 1. Standardized estimates for social capital and QoL mediated by HCP engagement

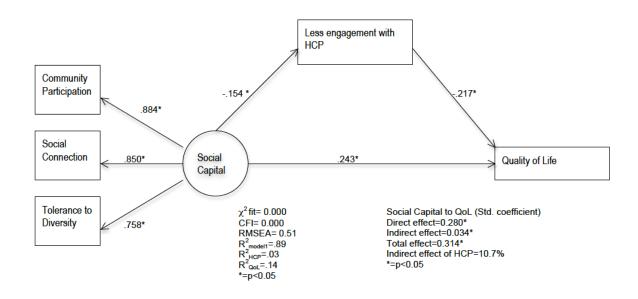
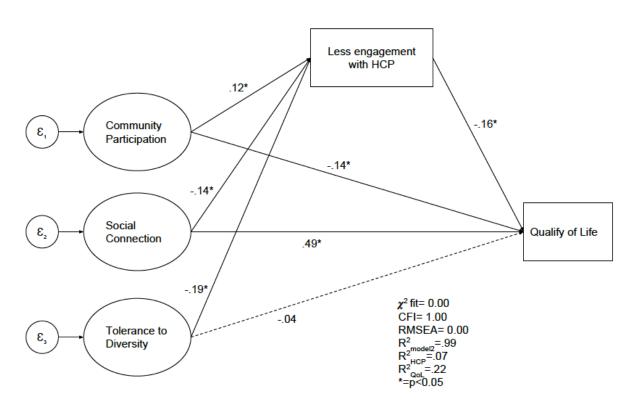


Figure 2.2 Model 2. Standardized estimates for 3 factors of social capital and QoL mediated by HCP engagement



Error terms(E) were corrected by creating latent variables and adjusting reliability of each factor (p.511, StataCorp, 2013)

References

- Acock, A. C. (2013). *Discovering structural equation modeling using stata*. Texas: Stata Press.
- Ahern, M. M., & Hendryx, M. S. (2003). Social capital and trust in providers. *Social Science & Medicine (1982), 57*(7), 1195-1203. doi:S027795360200494X [pii]
- Bakken, S., Holzemer, W. L., Brown, M. A., Powell-Cope, G. M., Turner, J. G., Inouye, J., . . . Corless, I. B. (2000). Relationships between perception of engagement with health care provider and demographic characteristics, health status, and adherence to therapeutic regimen in persons with HIV/AIDS. *AIDS Patient Care and STDs*, 14(4), 189-197. doi:10.1089/108729100317795
- Beach, M. C., Keruly, J., & Moore, R. D. (2006). Is the quality of the patient-provider relationship associated with better adherence and health outcomes for patients with HIV? *Journal of General Internal Medicine*, *21*(6), 661-665. doi:JGI399 [pii]
- Bourdieu, P. (1986). The forms of capital. In I. J. Richardson (Ed.), *Handbook of theory* and research for the sociology of education (pp. 241-258). New York: Greenwood.
- Centers for Disease Control and Prevention. (2011). *HIV surveillance report*. (No. vol.23.).
- Chi, B. H., Cantrell, R. A., Zulu, I., Mulenga, L. B., Levy, J. W., Tambatamba, B. C., . . . Stringer, J. S. (2009). Adherence to first-line antiretroviral therapy affects non-virologic outcomes among patients on treatment for more than 12 months in lusaka,

- zambia. International Journal of Epidemiology, 38(3), 746-756. doi:10.1093/ije/dyp004
- Dawson Rose, C., Webel, A., Sullivan, K. M., Cuca, Y. P., Wantland, D., Johnson, M.
 O., . . . Holzemer, W. L. (2014). Self-compassion and risk behavior among people living with HIV/AIDS. Research in Nursing & Health, 37(2), 98-106.
 doi:10.1002/nur.21587 [doi]
- Derose, K. P., & Varda, D. M. (2009). Social capital and health care access: A systematic review. *Medical Care Research and Review : MCRR*, *66*(3), 272-306. doi:10.1177/1077558708330428 [doi]
- Eller, L. S., Rivero-Mendez, M., Voss, J., Chen, W. T., Chaiphibalsarisdi, P., Iipinge, S., Brion, J. M. (2014). Depressive symptoms, self-esteem, HIV symptom management self-efficacy and self-compassion in people living with HIV. *AIDS*Care, 26(7), 795-803. doi:10.1080/09540121.2013.841842 [doi]
- Gregson, S., Mushati, P., Grusin, H., Nhamo, M., Schumacher, C., Skovdal, M., . . .

 Campbell, C. (2011). Social capital and women's reduced vulnerability to HIV infection in rural zimbabwe. *Population and Development Review, 37*(2), 333-359.
- Harpham, T., Grant, E., & Thomas, E. (2002). Measuring social capital within health surveys: Key issues. *Health Policy and Planning, 17*(1), 106-111.

- Holzemer, W. L. (2007). University of california, san francisco international nursing network for HIV/AIDS research. *International Nursing Review, 54*(3), 234-242. doi:10.1111/j.1466-7657.2007.00571.x
- Holzemer, W. L., Uys, L., Makoae, L., Stewart, A., Phetlhu, R., Dlamini, P. S., . . . Naidoo, J. (2007). A conceptual model of HIV/AIDS stigma from five african countries. *Journal of Advanced Nursing*, *58*(6), 541-551. doi:10.1111/j.1365-2648.2007.04244.x
- Hulley, S., Cummings, S., Browner, W., Grady, D., & Newman, T. (2007). *Designing clinical research* (third edition ed.). Philadelphia, USA: Lippincott Williams&Wilkins, Wolters Kluwer.
- Ion, A., Cai, W., Elston, D., Pullenayegum, E., Smaill, F., & Smieja, M. (2011). A comparison of the MOS-HIV and SF-12v2 for measuring health-related quality of life of men and women living with HIV/AIDS. AIDS Research and Therapy, 8(1), 5-6405-8-5. doi:10.1186/1742-6405-8-5 [doi]
- Kawachi, I., Kennedy, B. P., & Glass, R. (1999). Social capital and self-rated health: A contextual analysis. *American Journal of Public Health*, 89(8), 1187-1193.
- Kelley, J. M., Kraft-Todd, G., Schapira, L., Kossowsky, J., & Riess, H. (2014). The influence of the patient-clinician relationship on healthcare outcomes: A systematic review and meta-analysis of randomized controlled trials. *PloS One*, *9*(4), e94207. doi:10.1371/journal.pone.0094207 [doi]

- Kreuter. M, & Lezin. N. (2002). Social capital theory: Implications for community-based health promotion. In Diclemente. R, Crosby. R & Kegler. M (Eds.), *Emerging theories in health promotion practice and research: Strategies for improving public health* (first ed., pp. 228-254). San Francisco: Jossey-Bass.
- Luke, D. A., & Harris, J. K. (2007). Network analysis in public health: History, methods, and applications. *Annual Review of Public Health*, *28*, 69-93. doi:10.1146/annurev.publhealth.28.021406.144132
- Metcalfe, A., Lail, P., Ghali, W. A., & Sauve, R. S. (2011). The association between neighbourhoods and adverse birth outcomes: A systematic review and meta-analysis of multi-level studies. *Paediatric and Perinatal Epidemiology, 25*(3), 236-245. doi:10.1111/j.1365-3016.2011.01192.x; 10.1111/j.1365-3016.2011.01192.x
- Munro, B. H. (2005a). Confirmatory factor analysis. *Statistical methods for health care research* (5th ed., pp. 351). Philadelphia: Lippincott Williams & Wilkins.
- Munro, B. H. (2005b). Exploratory factor analysis. *Statistical methods for health care research* (5th ed., pp. 321). Philadelphia: Lippincott Williams & Wilkins.
- National Institutes of Health. (2001). Toward higher levels of analysis: Progress and promise in research on social and cultural dimensions of health. executive summary. (No. 21-5020).
- Onyx, J., & Bullen, P. (2000). Measuring social capital in five communities. *The Journal of Applied Behavioral Science*, *36*(1), 23-42. doi:10.1177/0021886300361002

- Putnam, R. D. (2001). Social capital: Measurement and consequences. *Isuma:*Canadian Journal of Policy Research, 2
- Renalds, A., Smith, T. H., & Hale, P. J. (2010). A systematic review of built environment and health. *Family & Community Health, 33*(1), 68-78. doi:10.1097/FCH.0b013e3181c4e2e5; 10.1097/FCH.0b013e3181c4e2e5
- Revicki, D. A., & Kaplan, R. M. (1993). Relationship between psychometric and utility-based approaches to the measurement of health-related quality of life. *Quality of Life Research: An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation*, 2(6), 477-487.
- Sivaram, S., Zelaya, C., Srikrishnan, A. K., Latkin, C., Go, V. F., Solomon, S., & Celentano, D. (2009). Associations between social capital and HIV stigma in chennai, india: Considerations for prevention intervention design. AIDS Education and Prevention: Official Publication of the International Society for AIDS Education, 21(3), 233-250. doi:10.1521/aeap.2009.21.3.233; 10.1521/aeap.2009.21.3.233
- Torres, E., Erwin, D. O., Trevino, M., & Jandorf, L. (2013). Understanding factors influencing latina women's screening behavior: A qualitative approach. *Health Education Research*, *28*(5), 772-783. doi:10.1093/her/cys106 [doi]
- Webel, A., Phillips, J. C., Rose, C. D., Holzemer, W. L., Chen, W. T., Tyer-Viola, L., . . . Salata, R. A. (2012). A cross-sectional description of social capital in an international sample of persons living with HIV/AIDS (PLWH). *BMC Public Health*, 12, 188-2458-12-188. doi:10.1186/1471-2458-12-188; 10.1186/1471-2458-12-188

Ziersch, A. M., Baum, F. E., Macdougall, C., & Putland, C. (2005). Neighbourhood life and social capital: The implications for health. *Social Science & Medicine (1982),* 60(1), 71-86. doi:10.1016/j.socscimed.2004.04.027

3 Chapter Three: Systematic review of meta-analysis: mobile phone reminders to retention to care at HIV clinics

3.1 Introduction

HIV remains a devastating disease and is ranked as the second cause of death in low-income countries (WHO, 2014). Worldwide, the adult prevalence of HIV is 0.8%; in Sub-Saharan Africa, the adult prevalence is as high as 16%. Sub-Saharan Africa is the epicenter of the HIV epidemic and is the region most affected by the disease (WHO, 2014). According to the Joint United Nations Programme on HIV/AIDS (UNAIDS), there were approximately 23.5 million people living with HIV in Sub-Saharan Africa. This accounts for 69% of the global HIV burden in 2011. HIV affects women disproportionally compared to men; 58% of those infected by HIV in this region are women (UNAIDS, 2012).

Universal access to HIV treatment, specifically anti-retroviral therapy (ART), has improved survival among people living with HIV/AIDS (PLWH). HIV is a condition requiring a lifetime of ART with close management by health care providers. In regions with good ART coverage, HIV has become a manageable chronic disease. One of the challenges in HIV prevention and management has been providing continuity of care, particularly in developing countries where the health care infrastructure is poor. The President's Emergency Plan for AIDS Relief (PEPFAR) recently reported that up to two-thirds of patients in developing countries may be lost to follow-up after HIV diagnosis and before starting ART (Rosen & Fox, 2011).

Mobile phone technology has become an important method for improving continuity of care for PLWH. At the end of 2013, there were as many registered mobile

devices as the number of people in the world. The diffusion of mobile technology has occurred faster in developing countries with 86% mobile cellular penetration rate. In 2012, there was at least one mobile phone line available in every household in Kenya (International Telecommunication Union, 2013; Rosen & Fox, 2011). Mobile phone technology, with its ubiquitous capability to reach people at a low cost can benefit health care systems in many developing countries, which are challenged by fragile infrastructure, health information system, and lack of human resources (Aranda-Jan, Mohutsiwa-Dibe, & Loukanova, 2014; Odeny et al., 2012). A limited number of studies have tested the use and effectiveness of mobile phones to improve health outcomes in resource limited settings. Acknowledging that providing continuity of care for PLWH is critical for HIV-related health outcomes, the purpose of this paper is to systematically review the effectiveness of mobile technology intervention, specifically mobile phone reminders, to improve patients' retention to care for HIV treatment.

3.1.1 Patient Retention in HIV Care: Challenges and Consequences

Non-attendance at health care appointments is a significant independent predictor of progression of HIV (Berg et al., 2005a). Non-adherence to medications leads to progression of HIV disease, posing a higher risk of transmitting HIV to others in the community (Berg et al., 2005a; Gardner, McLees, Steiner, Del Rio, & Burman, 2011). Authors of a retrospective cohort study identified that HIV patients with poorer retention to care were more likely to have poorer survival over time, less improvement of CD4 cell counts and less reduction in plasma HIV level than those adhering to HIV care (Giordano et al., 2007). Obviously, people who do not return for periodic appointments are eventually LTFU. A meta-analysis reported that retention rate for PLWH into care

was 62% in 3 years in the United States (Gardner et al., 2011; Marks, Gardner, Craw, & Crepaz, 2010). Gardner et al. estimated that less than 50 percent of PLWH in the United States are actively engaged in HIV care, and only 19% of PLWH have an undetectable HIV viral load (Gardner et al., 2011). The rate of LTFU in treatment programs varies widely based on setting, ranging from 5 to 40 percent within 6 months of ART initiation in resource-limited settings (Losina et al., 2009).

Several terms are often used interchangeably to describe patients' retention to care and provision of continuity of care: missed appointments, non-attendance, and LTFU (lost to follow-up). Missed appointments and non-attendance are usually treated as binary outcomes, defined as not showing up at the clinic at the given appointment date and time without informing the clinic. Chi and the colleagues defined LTFU as 'patient does not present to medical appointment within 180 days from the last clinic visit', and used this definition to describe retention to care among HIV patients attending 111 health facilities in 19 countries (Chi et al., 2011). In other studies, measuring attendance is defined as returning to care within a certain interval ranging from 3 days to 9 months (Bourne et al., 2011; Odeny et al., 2012). The present literature review acknowledges a wide variation in definition of attendance, and uses the definitions as specified by each authors as LTFU.

Reasons for LTFU are multi-factorial, and differ based on ability to access resources. In resource-limited settings, including many African rural areas, lack of transportation and cost of travel has been identified as barriers to retention to HIV care. In one study from Kenya, participants who had to pay more than US\$1.25 for transportation to a clinic were more likely to fail to return for care compared to those

paid less than that amount (RR: 1.35, 95% CI 1.15-1.58) (Odeny et al., 2012). This is consistent with other study findings about distance from clinic; people who lived closer to the hospital were more likely to return to the hospital to get their CD4 counts (Kliner, Knight, Mamvura, Wright, & Walley, 2013). A qualitative study from Ethiopia identified substance use, along with HIV associated stigma, as two principle reasons for LTFU (Bezabhe et al., 2014). The authors of a retrospective cohort study in South Africa with PLWH who started ARV treatment found that gender, ethnicity, and age were not associated with LTFU. Rather, nearly half of the patients who were LTFU died, relocated or transferred to other clinics (Dalal et al., 2008).

In higher resource settings, gender and age are two important factors associated with LTFU. A randomized controlled study in Switzerland conducted in large urban primary care and HIV clinics found that younger age, male sex, follow-up appointment greater than 1 year, and substance abuse were significant predictors for LTFU (Perron et al., 2010). Other patient-related factors are health beliefs, health status, transportation, scheduling, and financial status. Lack of communication between providers and patients, waiting time at clinic, and quality of consultations are additional health care related factors that impact LTFU (Car, Gurol-Urganci, de Jongh, Vodopivec-Jamsek, & Atun, 2012).

A review of U.S. studies suggested multiple strategies to improve retention to care of HIV patients, such as facilitating access to care (e.g. transportation services), care management, peer support, and promoting diversity in clinical care (e.g. bilingual/bicultural services) (Higa, Marks, Crepaz, Liau, & Lyles, 2012). A randomized controlled study from Malawi used incentives to encourage people to return to the clinic

to receive their HIV test results. Thirty-four percent of people returned from the non-incentive group; even a small incentive doubled the return rates (Thornton, 2008).

3.1.2 Mobile technologies, an affordable, innovative approach to improving retention to HIV care

Mobile phone subscriptions have almost saturated the globe. With a world population of over 7.2 billion people, there were 6.8 billion mobile subscriptions in 2013. This phenomenon has been reported in several research studies. Three studies from rural Uganda, Kenya and rural Swaziland reported that the proportion of cell-phone ownership among screened participants reached 65 to 75% (Kliner et al., 2013; Kunutsor et al., 2010; Odeny et al., 2012).

Compared to phone calls, which can be relatively costly for low-income subscribers, text messages or short message service (SMS) are more affordable with less interruption of recipients' daily life. SMS can be stored and accessed later (Coomes et al., 2012). With the fast penetration of mobile phone subscription in developing countries, studies have used mobile technologies to assess a range of health outcomes, such as medication adherence, monitoring chronic health outcomes, and providing psychological support (Car et al., 2012). A recent meta-analysis that included 9 intervention studies showed that SMS reminders improved adherence to ART. PLWH who received SMS reminders had significantly higher ART adherence (pooled odd ratio (OR) = 1.39; 95% confidence interval (CI) = 1.18, 1.64) and lower HIV RNA load (pooled OR=1.56; 95% CI=1.11, 2.20) compared to the control group (Finitsis, Pellowski, & Johnson, 2014). A Cochrane review of four intervention studies concluded that SMS

reminders of general health care appointments showed moderate effectiveness on clinic attendance (pooled risk ratio (RR): 1.10; 95% CI=1.03, 1.17) (Car et al., 2012).

In addition to improved patient health outcomes, mobile technologies assist health care delivery by providing a platform for staff training, disease surveillance, data collection and reporting, and monitoring of drug supply chains (Aranda-Jan et al., 2014). This innovative approach has the potential to fill gaps in health care delivery in many developing countries.

3.1.3 Significance of This Paper

Despite the rapidly increasing research on the use of mobile technologies for improved health outcomes, it is not clear whether mobile phone reminders can prevent LTFU and improve retention to care among PLWH. While its effectiveness on adherence to ART is promising, individuals outside of care or LTFU do not benefit from the intervention.

Considering that one of the biggest challenges in the provision of HIV care is linkage to care from diagnosis to life-long commitment to ART adherence, understanding mobile phone effectiveness on retention to care is critical. Using a systematic review, meta-analysis approach, we answer the following three research questions: (1) what is the available clinical research evidence on mobile phone reminders for retention to HIV care? (2) what is the effect size of an mobile phone reminders intervention?, and (3) what are the implications of these findings to future studies?

3.2 Methods

3.2.1 Search Strategies

We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement guidelines (Moher, Liberati, Tetzlaff, Altman, & PRISMA Group,

2009). The authors (SJ and YC) conducted an initial literature search using Boolean strategy using the following databases: PubMed, CINAHL, ProQuest, and Web of science. Search terms were 'HIV AND mobile phone, cellular phone, text message* OR SMS (short message service)'. Databases were searched between March 28 and April 26, 2014 with a second search in November 2015 for possible inclusion of additional studies. There was no restriction based on language or year published although most of the literature was from the last 15 years due to the nature of mobile technology used in health care research. The searches resulted in 1,438 peer-reviewed articles (see figure 3.1). SJ and YC independently reviewed the abstracts and screened duplications of the articles using a citation management program (RefWorks/EndNote). Inclusion criteria for the final reviewed papers were: 1) clinical research employing mobile phone reminders to improve retention to care; and 2) inclusion of HIV patients and family member paired with babies exposed to HIV. Study protocols or review articles were excluded.

3.2.2 Data collection

SJ manually extracted data from full scripts of selected articles using a standardized extraction form. The form includes general information about the study (author, year of published, study location and study period), study design (types of study design and control for threat to validity), sample characteristics (age, gender, race/ethnicity), types of intervention, outcome variables (measurement and parameter of outcome variable, effect size, p-value, 95% CI), statistical methods used in the studies, and appraisal of strengths and weakness of the studies. For studies having HIV patients as a subgroup of a larger study sample, the subgroup data were primarily used. SJ extracted and calculated the odd ratio (OR) and 95% CI to obtain the effect size of the intervention

(Lipsey & Wilson, 2001). To improve the consistency between the studies, for studies that employed more than one intervention arm, the OR based on mobile text message reminder intervention was compared to standard care. For longitudinal studies, data from the last measurement period was used to evaluate the sustainability of the intervention.

3.2.3 Data analysis

In order to assess heterogeneity between study results, the I-squared statistic was used to inform the method of meta-analysis. In the preliminary analysis, the I-squared values were 94.1% (heterogeneity chi-squared= 136.41 (d.f.=8), p<0.001), suggesting study heterogeneity, and the need to use a random effects model of analysis to obtain overall effect sizes (ES). The random effects model assumes that the variability of ES across the studies is attributable not only to sample errors at the subject-level but to other unmeasured sources of error. This leads to a wider 95% CI for the ES using a random effect model (Higgins, Thompson, Deeks, & Altman, 2003; Lipsey & Wilson, 2001). Funnel plots were evaluated for publication bias together with statistical tests (Egger's and Begg's tests). Stata 13 was used for analysis.

3.2.4 Study Outcomes: LTFU and Non-Attendance Rate

Given that studies were conducted with participants in HIV health care settings, the proportion of attendance at follow-up appointments was the primary outcome for the studies reviewed. In other words, non-attendance is used as a proxy measure for LTFU. The proportion of non-attendance is inherently a dichotomous variable. Therefore, the OR is used to calculate the effect size. Attendance was extracted from and confirmed

by patients' medical charts or clinic records. Attendance was counted as returning to care within a time frame as determined by study authors.

3.3 Results

3.3.1 Study Design and Types of SMS Reminders

All nine studies were conducted within the past 5 years, ranging from April 2010 to April 2015 (Table 3.1). Five RCTs and four before and after controlled studies were included in the final analysis. Before and after controlled studies were conducted at the clinic level to test the effectiveness of the mobile phone reminder intervention. Post-intervention groups were compared to pre-intervention groups, although the members in the two groups were different. Study settings were HIV clinics or hospitals from United States (US), Switzerland, United Kingdom (UK), Kenya, Cameroon, South Africa and Swaziland.

The pooled sample size was a total of 3,004 participants. Study participants were adult patients with HIV or HIV-exposed babies paired with their mothers with HIV. For example, a study from Kenya implemented mobile phone reminders for HIV positive mothers to alert test results availability and clinic appointments for their babies exposed to HIV during birth. The unit of analysis for this study was the mother/caregiver and baby dyad. Sample characteristics are limited because one study (Perron et al., 2010) did not provide any demographic information for HIV sub-group, which have used in this review. Approximately 79.7% of the pooled sample were women and the median age of the sample was 34.6 years old.

Types of mobile phone reminders are divided into two categories: (1) appointment reminders, one or two days prior to the appointments using SMS or mobile

phone calls; and (2) sequential reminders including SMS, mobile phone calls, and postal reminders. The content of the reminders was not individualized. Examples of SMS from these studies were "come back to clinic" or "Remember: you have a doctor's appointment tomorrow". SMS were usually delivered once without confirmation of whether participants actually received the message or not.

3.3.2 Review of the studies

While all study interventions were automated text message reminders, Kliner et al. (2013) implemented 'buzzing' text message reminders at no cost to the patient and the clinic (Kliner et al., 2013). The message received by the patient registered the hospital's number as 'go to hospital' on participants' mobile phones. However, the intervention did not increase return rates to the hospital to collect CD4 count results. The reminder maintained patient privacy, yet lacked specific reminder messages.

Norton and the colleagues used mobile phone text message reminders to PLWH to improve retention to care in the United States. The intervention group (n= 25) received a text message and the control group (n=27) received the standard care procedure, an automated reminder phone call to a landline. The study had a high participant refusal rate (45%) at screening and a high attrition rate (28%) in the intervention group. This resulted in small sample size and low statistical power; this RCT did not detect efficacy of the mobile text message reminder to improve retention to care (Norton et al., 2014).

The efficacy of mobile phone reminders was established among patients attending primary care clinics in Geneva (Perron et al., 2010) and a sexual health clinic in London (Farmer, Brook, McSorley, Murphy, & Mohamed, 2014). Overall missed

appointment rates dropped by four percent (p<0.005) in the clinic after the intervention. Male sexual health clinic attendants were more likely to return to care than females and PLWH (10%, p<0.05) (Farmer et al., 2014). For the total sample, the missed appointment rate was lower (7.8%) among the intervention group, compared to 11.4% (p<0.005) in the usual care group (Perron et al., 2010). However, when sub-group analysis was performed with PLWH, the intervention did not improve clinic attendance (Farmer et al., 2014; Perron et al., 2010).

Five studies used mobile phone reminders to target mothers with HIV to improve retention to a prevention of mother to child transmission program (PMTCT) or to follow up with babies who were exposed to HIV during birth (Bigna, Noubiap, Kouanfack, Plottel, & Koulla-Shiro, 2014; Finocchario-Kessler et al., 2014; Kebaya, Nduati, Wamalwa, Kariuki, & Bashir, 2014; Odeny et al., 2014; Schwartz et al., 2015). All five of the studies are from Africa and targeted retention to postnatal care and early diagnose of HIV of the babies exposed to HIV. Four studies concluded that mobile phone reminders significantly improved the outcomes (See table 3.1, Figure 3.4). Schwartz and colleagues' before and after controlled study did not find that weekly mobile phone reminders significantly improved postnatal women's returning to care(Schwartz et al., 2015).

Based on our systematic review, four studies were excluded from the metaanalysis because they enrolled participants at risk for HIV, but who did not have HIV. Three studies (Bourne et al., 2011; Burton, Brook, McSorley, & Murphy, 2014; Zou et al., 2013) were similar to each other in study design, settings and population and were conducted in large, urban sexual health clinics in developed countries (Table 3.2). The samples were drawn from population at high risk for HIV based on their sexual health history, and mainly consisted of young men who had sex with men. Odeny et al. (2012) conducted a two-arm RCT in Kenya that we also excluded because the study targeted adult males who underwent circumcision as a measure of HIV prevention. The intervention group received daily informative text messages on post-circumcision care and reminders to return for follow-up appointment. This group was more likely to return to care (RR=1.09, 95% CI=1.00-1.20, P<0.05) compared to those men who didn't receive an SMS message (Odeny et al., 2012).

3.3.3 The Effectiveness of Mobile Phone Reminders

A random effects model was used to present overall effect of the mobile phone reminder intervention among PLWH in 9 studies (Figure 3.2). Mobile phone reminders improved clinic attendance at follow-up appointments compared to usual care among PLWH (pooled OR=2.04, 95% CI: 0.97-4.27).

Figure 3.3 shows funnel plot of the nine studies. There is no evidence of publication bias but small study effect exists (Eger's p=0.647, Begg's p=0.835).

3.3.4 Sub-group analysis

A sub-group analysis was conducted with the six studies (four RCTs and two before and after controlled studies) from Africa (n=2,182). Ninety percent of the pooled sample were women, because the five out of six studies were carried out at PMTCT or post-natal clinic settings. PLWH who received mobile phone reminders were about three times more likely to return to care than those in usual care (pooled OR=2.92, 95% CI: 1.13-7.53) (see figure 3.4). The analysis with three studies (two RCTs and one before and after study) from UK, U.S., and Switzerland (n=822) did not show a statistically

significant difference between groups who received mobile phone reminders and those who received standard care (pooled OR=1.16, 95% CI: 0.95-1.42).

Another subgroup analysis was conducted after excluding the 4 before and after studies (Figure 3.5). The pooled sample for the five RCTs is 1,135 (Bigna, Kouanfack, Noubiap, Plottel, & Koulla-Shiro, 2013; Kebaya et al., 2014; Norton et al., 2014; Odeny et al., 2014; Perron et al., 2010). Mobile phone reminders significantly improved clinic attendance compared to usual care (pooled OR=2.04, 95% CI: 1.11-3.74).

3.4 Discussion

This is the first systematic review and meta-analysis to assess the efficacy of mobile phone reminders to improve retention to care among PLWH in both high- and low-income countries. We found that PLWH who received mobile phone reminders for their follow-up appointments were two times more likely to return to the care than those who didn't receive reminders; however, this estimate was not statistically significant. Our sub-group analysis of 5 RCTs showed a significant effect of mobile phone reminders and 6 studies in Africa found that PLWH, mostly women with HIV who received mobile phone reminders were three times more likely to return to care than those who received no reminders, and these findings were statistically significant.

Mobile phone reminders are an effective intervention in resource-limited settings. Our study findings are consistent with the Cochrane review of mobile phone reminders on follow up appointments among a general population. The review included four RCTs conducted in various health care settings ranging from health promotion centers, primary care clinics, and ENT clinics from four mid- to high-income countries. The review concluded that mobile phone reminders had a low to moderate effect in

improving clinic attendance, based on three RCTs of moderate quality (RR: 1.10; 95% CI=1.03, 1.17) (Car et al., 2012).

Mobile phone reminders address 'patient forgetfulness', and may mitigate LTFU by providing simple reminders using mobile phones. However, LTFU, or poor retention to care, is multi-factorial, and these reasons differ depending on whether PLWH live in high- or low-income countries. In Swaziland, patients who were eligible to start ART tended to return for follow-up because of the symptoms they experienced (Kliner et al., 2013). In Ethiopia, Bezabhe and colleagues used qualitative interviews among 24 patients and identified three facilitators of retention to care —disclosure of HIV status, social support, and use of reminder aids (Bezabhe et al., 2014). Therefore, mobile phone reminders will be more effective when they address multifaceted issues, such as signs and symptoms that prompt a clinic visit.

None of the reviewed studies reported use of theoretical frameworks to guide the intervention. Despite usefulness of theory to guide interventions, research study design, and data collection and analysis, studies often underestimate how theory can increase understanding of why an effect is occurring or not (Reeves, Kuper, & Hodges, 2008). Coomes et al. proposed a conceptual framework for 'integrating the communication functionality of SMS with important psychosocial factors that could mediate the impact of SMS communication on health outcomes' (Coomes et al., 2012). This model suggests that the SMS intervention is a helpful tool to improve healthcare quality, as well as patient health outcomes, when SMS is interactive, when content is personalized, and when timing of the SMS is factored into to the intervention (Coomes et al., 2012). Similarly, Finitsis and colleagues' meta-analysis found that SMS interventions had

larger effects when messages are sent less frequently than daily, allow for bidirectional communication, and are personalized messages tailored to patients' needs (Finitsis et al., 2014).

There are several limitations to the present analysis. First, the analysis was not limited to RCTs, which limits our ability to state that the SMS intervention, in and of itself, improves retention to HIV care. Second, the sample size (n=9) is small and studies were heterogeneous. Finally, every study required mobile phone ownership in order to be eligible for study participation. Thus, findings are not generalizable to the non-mobile phone owners, who may be the most marginalized and most likely to be non-adherent to clinic visits. It is important to note that pooled analysis is mainly based on women with HIV from resource-limited settings. Therefore, our findings may not generalize to men with HIV or PLWH in high-income countries.

There are several studies from South Africa, Kenya, Swaziland, Mozambique, Malawi and United States that are currently testing mobile phone reminders on retention to HIV care (Bassett et al., 2013; Christopoulos et al., 2014; Elul et al., 2014; McNairy et al., 2015; Mwapasa et al., 2014; van der Kop et al., 2013). A two-armed RCT in the US is currently testing SMS reminders boosted with informational, supportive, and motivational messages on retention to care and virological suppression of HIV. This study is based on behavioral theory and it testing cost-effectiveness of the intervention (Christopoulos et al., 2014). All of these studies will add to the body of literature on SMS on retention to care.

3.5 Conclusion

Sub-optimal adherence to HIV care can lead to ART drug resistance, and this has become a threat to the health of PLWH (Berg et al., 2005b; Finitsis et al., 2014). Mobile phone reminders are a relatively new and innovative approach in HIV care, but the body of evidence to date is inconclusive about the impact of SMS on clinic attendance and HIV health outcomes across settings. We found a strong effect of mobile phone reminders to improve PLWH's attendance to care in resource limited settings, mostly among women with young infants.

With the ubiquitous ownership of mobile phones globally, including among people living in low-income countries, mobile phone reminders to return to clinic for care are feasible. Future studies should examine the impact of incentivized SMS reminder interventions on access to health services and improved HIV health outcomes.

Messages should be designed to allow for bidirectional conversations, be tailored for individual needs and should serve as a bridge to other healthcare and social support resources. The ultimate goal of SMS reminders is not only to improve retention to HIV care, but to improve the quality of life of people living with HIV around the world.

Table 3.1 Review of the Studies

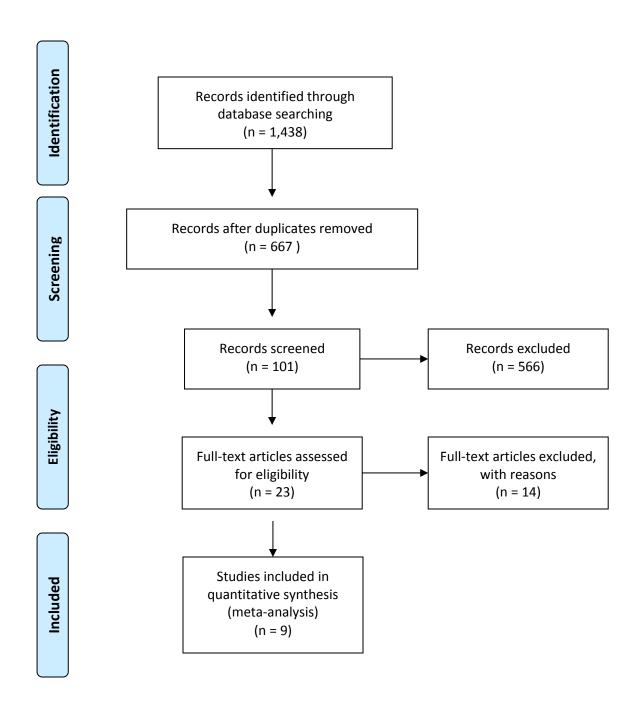
1 st Author (year)	Location	Sample	Design	Intervention	Measures	Findings
Perron (2010) Study dates: 04/10-06/10	Urban HIV ambulatory clinic, Geneva, Switzerland	Vulnerable population/ undocumented migrants, asylum seekers, immigrants with HIV (n=303), HIV subgroup demographic info: NA	Randomized Controlled Trial (RCT)	Sequential reminders: phone call->SMS- >postal reminders VS no reminders 2 days prior to the appointment	Rate of missed appointment in the clinics	Intervention: 12.7%, Control: 15% (p=0.62)
Kliner (2013) Study dates: 03/13	Regional hospital, rural Lubombo, Swaziland	People with recent HIV diagnosis (n=459, male=210, female=249, mean age=33)	Before and after study	Buzz message* reminder sent 1 day prior to appointment: CD4 cell counts result collection VS no reminder	Rate of attendance at the HIV testing and counseling department	Intervention: 83.3%, Control: 80.1% (p=0.40) No effect
Bigna (2014) Study dates: 01/13-05/13	Multisite: urban, semi- urban, and rural HIV clinics in Cameroon	Care givers of children with or exposed to HIV (n=242 adult-child pairs, male=37, female=205, age=43)	RCT	SMS & phone call, SMS, phone call, or no reminders (control) 2-3 days prior to the appointment	Proportion of patients attending a schedule appointment	SMS & phone call (89%), SMS (75%), phone call (85%), or control (51%) OR=2.9 (SMS vs control) OR=4.7(inter vention vs control)
Farmer (2014) Study dates: 05/12-04/13	Sexual health clinic, London, UK	Young adults with HIV* (n=467, median age=45, male=263, female=204). *Demographic info obtained through corresponding	Before and after study	SMS reminder 2 days prior to follow-up appointment	Rate of attendance for 12 months before/after the intervention	Intervention: 75%, Control: 72% (p>0.05)
Finocchario- Kessler (2014) Study dates: 06/11-05/12	Urban and peri-urban hospital, Kenya	HIV mother and infant who exposed to HIV pair (n=843, all female, mean age=30)	Before and after study	EID (early infant diagnosis): text message reminders to mothers' cell phone to alert test results and clinic appointments	Retention to EID: the proportion of infants engaged in EID care by 9 months postnatal	Intervention: 93.6%, before intervention: 44.2%

1st Author (year)	Location	Sample	Design	Intervention	Measures	Findings
Norton (2014) Study dates: 06/10-08/10	Urban HIV clinic, North Carolina, USA	HIV patients with access to SMS (n=52, male=39, female=13, mean age=44)	RCT	SMS reminder 1 day prior to appointment plus standard care VS standard care (automated phone reminder when home phone is available)	Rate of clinic attendance	Intervention: 72.0%, Control: 81.0% (p=0.42) No effect
Odeny (2014) Study dates: 05/13-07/13	5 health facilities, Nyanza, Kenya	Pregnant women with HIV, >18 years old (n=388, median age=28)	2 arm, unblinded RCT	14 weekly, automated SMS prenatal and post-partum	Rate of women attending maternal postpartum clinic& early infant HIV testing	Intervention: 19.6%, Control: 11.8% (relative risk=1.66, 95% CI=1.02-2.70) Intervention: 92.0%, Control: 85.1% (relative risk=1.08, 95% CI=1.00-1.16)
Kebaya (2015) Study dates: n/a	3 health facilities, Western Kenya	Postnatal women with HIV (n=150, mean age=26)	RCT	Bi-weekly mobile phone call reminders	Proportion of women retaining at PMTCT	Intervention: 69.4%, Control: 37.3% (p<0.001)
Schwartz (2015) Study dates: 05/13-07/13	Primary care clinic, South Africa	Pregnant women with HIV (>36 weeks of gestation) (n=100, median age=28)	Before and after study	Weekly, prescripted text messages for 8 weeks plus 3 phone calls (1 pre and 2 post- delivery) regarding postpartum care and reminder to return to care with baby at 6 weeks	Proportion of women retaining at care/ART pick-up at 10 weeks and 12 months	Intervention: 94%, pre- intervention: 96% (p=0.65) at 10 weeks Intervention: 78%, pre- intervention: 76% (p=0.71) at 12 months

Table 3.2 Review of excluded studies with reasons

1 st Author (year)	Location	Sample	Design	Intervention	Findings (Attendance rates)	Reason for exclusion
Bourne (2011) Conducted in 2009	Public STI clinic Australia	Men who have sex with men (MSM) (n=1,978)	Before and after operational study	SMS reminder to return for retesting STIs/HIV after 3- 6 months	Intervention: 64.4%, Control: 29.7% (p<0.05)	
Burton (2014) Conducted in 2012	STI clinic United Kingdom	demographic information At higher risk of STIs and HIV (n=539) male=243 (45.5%) female=296 (54.5%)	Controlled before and after study	SMS reminder to return for retesting STIs/HIV after 6 wks	Intervention: 32.5%, Control: 35.5% (p=0.78)	
Farmer (2014)* Conducted in 2012-13	Sexual health clinic United Kingdom	Young adults (n (cases)=3,717) No demographic information	Before and after study	SMS reminder 2 days prior to pre- booked appointments	Intervention: 76%, Control: 72% (p<0.05)	Not meeting inclusion
Odeny (2012) Conducted in 2010-11	12 male circumcision sites Nyanza province, Kenya	Male undergoing circumcision for HIV prevention (n=1,200) Age: mean 25 years	Two-arm, RCT	Automated daily SMS reminder for 7 post-op days in patients preferred languages	Intervention: 65.4%, Control: 59.7% (p<0.05)	Primary care clinic attendees or Risk for STI/HIV not PLWH
Perron (2010)* Conducted in 2010	Urban primary ambulatory clinic Switzerland	Vulnerable population (n=2123) male=55.5%, female=44.5% Age: mean (SD) 46 years (18.2)	Randomized Controlled Trial (RCT)	Sequential reminders: phone call->SMS- >postal reminders VS no reminders 2 days prior to the appointment	Intervention: 93.2%, Control: 88.6% (p<0.05)	
Zou (2013) Conducted in 2010	Public sexual health clinic Australia	MSM (n=2,397) No demographic information	Retrospective, controlled before and after study	SMS or email (or both) reminder for retesting STIs at 3,6,12 months per participants' request by Computer Assisted Self- Interview (CASI) system	Intervention: 88.9%, Control: 70.8% (p<0.05)	

Figure 3.1 Literature search results



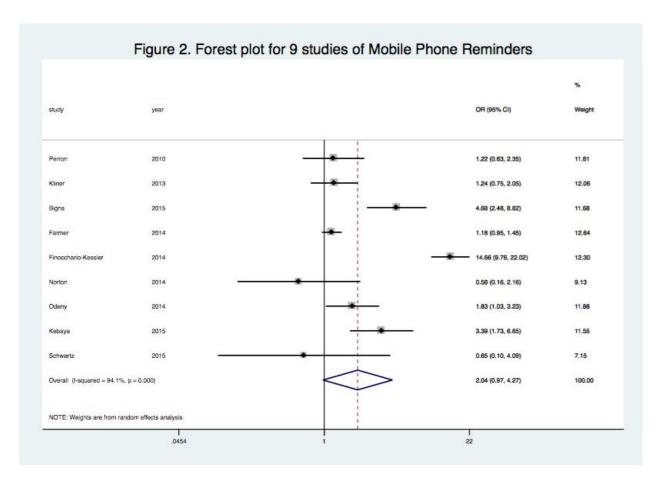


Figure 3.2 Forest plot for 9 studies of mobile phone reminders

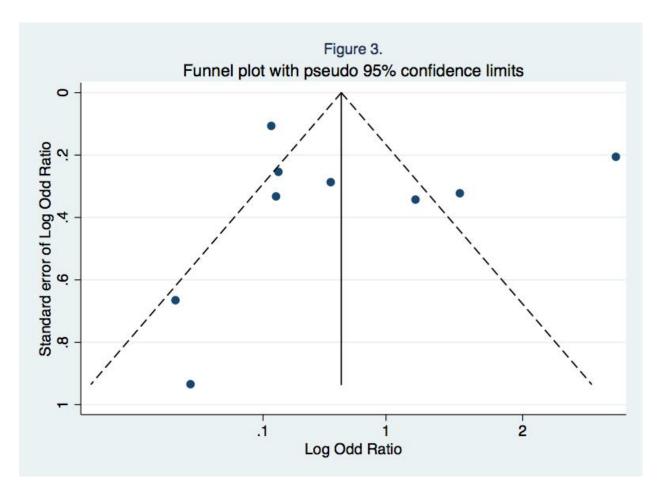


Figure 3.3 Funnel plot with pseudo 95% confidence limits

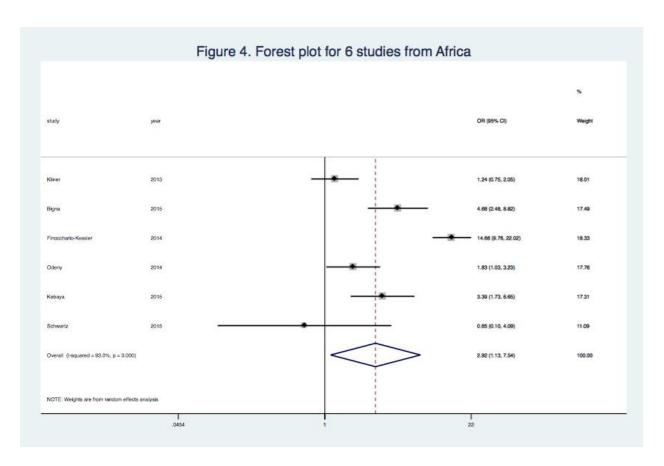


Figure 3.4 Forest plot for 6 studies from Africa

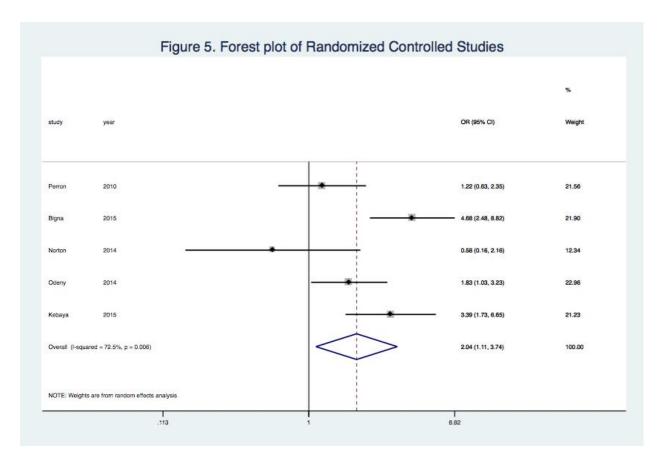


Figure 3.5 Forest plot of randomized controlled studies

References

- Aranda-Jan, C. B., Mohutsiwa-Dibe, N., & Loukanova, S. (2014). Systematic review on what works, what does not work and why of implementation of mobile health (mHealth) projects in africa. *Bmc Public Health, 14*, 188. doi:10.1186/1471-2458-14-188
- Bassett, I. V., Giddy, J., Chaisson, C. E., Ross, D., Bogart, L. M., Coleman, S. M., . . . Losina, E. (2013). A randomized trial to optimize HIV/TB care in south africa:

 Design of the sizanani trial. *Bmc Infectious Diseases, 13*, 390. doi:10.1186/1471-2334-13-390
- Berg, M. B., Safren, S. A., Mimiaga, M. J., Grasso, C., Boswell, S., & Mayer, K. H. (2005a). Nonadherence to medical appointments is associated with increased plasma HIV RNA and decreased CD4 cell counts in a community-based HIV primary care clinic. *AIDS Care*, *17*(7), 902-907. doi:W74171324K2312M1 [pii]
- Berg, M. B., Safren, S. A., Mimiaga, M. J., Grasso, C., Boswell, S., & Mayer, K. H. (2005b). Nonadherence to medical appointments is associated with increased plasma HIV RNA and decreased CD4 cell counts in a community-based HIV primary care clinic. *AIDS Care*, *17*(7), 902-907. doi:W74171324K2312M1 [pii]
- Bezabhe, W. M., Chalmers, L., Bereznicki, L. R., Peterson, G. M., Bimirew, M. A., & Kassie, D. M. (2014). Barriers and facilitators of adherence to antiretroviral drug therapy and retention in care among adult HIV-positive patients: A qualitative study from ethiopia. *PloS One*, *9*(5), e97353. doi:10.1371/journal.pone.0097353 [doi]

- Bigna, J. J. R., Kouanfack, C., Noubiap, J. J. N., Plottel, C. S., & Koulla-Shiro, S. (2013). A randomized blinded controlled trial of mobile phone reminders on the follow-up medical care of HIV-exposed and HIV-infected children in cameroon: Study protocol (MORE CARE). *Trials*, *14*, 313. doi:10.1186/1745-6215-14-313
- Bigna, J. J. R., Noubiap, J. J. N., Kouanfack, C., Plottel, C. S., & Koulla-Shiro, S. (2014). Effect of mobile phone reminders on follow-up medical care of children exposed to or infected with HIV in cameroon (MORE CARE): A multicentre, single-blind, factorial, randomised controlled trial. *The Lancet Infectious Diseases, 14*(7), 600-608. doi:http://dx.doi.org/10.1016/S1473-3099(14)70741-8
- Bourne, C., Knight, V., Guy, R., Wand, H., Lu, H., & McNulty, A. (2011). Short message service reminder intervention doubles sexually transmitted infection/HIV re-testing rates among men who have sex with men. *Sexually Transmitted Infections*, *87*(3), 229-231. doi:10.1136/sti.2010.048397; 10.1136/sti.2010.048397
- Burton, J., Brook, G., McSorley, J., & Murphy, S. (2014). The utility of short message service (SMS) texts to remind patients at higher risk of STIs and HIV to reattend for testing: A controlled before and after study. *Sexually Transmitted Infections*, *90*(1), 11-13. doi:10.1136/sextrans-2013-051228: 10.1136/sextrans-2013-051228
- Car, J., Gurol-Urganci, I., de Jongh, T., Vodopivec-Jamsek, V., & Atun, R. (2012).

 Mobile phone messaging reminders for attendance at healthcare appointments. *The Cochrane Database of Systematic Reviews, 7*, CD007458.

 doi:10.1002/14651858.CD007458.pub2; 10.1002/14651858.CD007458.pub2

- Chi, B. H., Yiannoutsos, C. T., Westfall, A. O., Newman, J. E., Zhou, J., Cesar, C., . . .

 International Epidemiologic Databases to Evaluate AIDS Collaboration. (2011).

 Universal definition of loss to follow-up in HIV treatment programs: A statistical analysis of 111 facilities in africa, asia, and latin america. *PLoS Medicine*, 8(10), e1001111. doi:10.1371/journal.pmed.1001111 [doi]
- Christopoulos, K. A., Riley, E. D., Tulsky, J., Carrico, A. W., Moskowitz, J. T., Wilson, L., . . . Hilton, J. F. (2014). A text messaging intervention to improve retention in care and virologic suppression in a U.S. urban safety-net HIV clinic: Study protocol for the Connect4Care (C4C) randomized controlled trial. *BMC Infectious Diseases, 14*, 718-014-0718-6. doi:10.1186/s12879-014-0718-6 [doi]
- Coomes, C. M., Lewis, M. A., Uhrig, J. D., Furberg, R. D., Harris, J. L., & Bann, C. M. (2012). Beyond reminders: A conceptual framework for using short message service to promote prevention and improve healthcare quality and clinical outcomes for people living with HIV. AIDS Care, 24(3), 348-357.
 doi:10.1080/09540121.2011.608421 [doi]
- Dalal, R. P., Macphail, C., Mqhayi, M., Wing, J., Feldman, C., Chersich, M. F., & Venter, W. D. (2008). Characteristics and outcomes of adult patients lost to follow-up at an antiretroviral treatment clinic in johannesburg, south africa. *Journal of Acquired Immune Deficiency Syndromes* (1999), 47(1), 101-107.
 doi:10.1097/QAI.0b013e31815b833a [doi]

- Elul, B., Lahuerta, M., Abacassamo, F., Lamb, M. R., Ahoua, L., McNairy, M. L., . . . Jani, I. (2014). A combination strategy for enhancing linkage to and retention in HIV care among adults newly diagnosed with HIV in mozambique: Study protocol for a site-randomized implementation science study. *BMC Infectious Diseases, 14*, 549-014-0549-5. doi:10.1186/s12879-014-0549-5 [doi]
- Farmer, T., Brook, G., McSorley, J., Murphy, S., & Mohamed, A. (2014). Using short message service text reminders to reduce 'did not attend' rates in sexual health and HIV appointment clinics. *International Journal of STD & AIDS, 25*(4), 289-293. doi:10.1177/0956462413502325; 10.1177/0956462413502325
- 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; 10.1371/journal.pone.0088166
- Finocchario-Kessler, S., Gautney, B. J., Khamadi, S., Okoth, V., Goggin, K., Spinler, J. K., . . . HITSystem Team. (2014). If you text them, they will come: Using the HIV infant tracking system to improve early infant diagnosis quality and retention in kenya. *AIDS (London, England), 28 Suppl 3*, S313-21. doi:10.1097/QAD.0000000000000332 [doi]
- Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clinical Infectious Diseases : An Official Publication*

- of the Infectious Diseases Society of America, 52(6), 793-800. doi:10.1093/cid/ciq243 [doi]
- Giordano, T. P., Gifford, A. L., White, A. C., Jr, Suarez-Almazor, M. E., Rabeneck, L., Hartman, C., . . . Morgan, R. O. (2007). Retention in care: A challenge to survival with HIV infection. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America, 44*(11), 1493-1499. doi:CID41288 [pii]
- Higa, D. H., Marks, G., Crepaz, N., Liau, A., & Lyles, C. M. (2012). Interventions to improve retention in HIV primary care: A systematic review of U.S. studies. *Current HIV/AIDS Reports*, 9(4), 313-325. doi:10.1007/s11904-012-0136-6 [doi]
- Higgins, J. P., Thompson, S. G., Deeks, J. J., & Altman, D. G. (2003). Measuring inconsistency in meta-analyses. *BMJ (Clinical Research Ed.), 327*(7414), 557-560. doi:10.1136/bmj.327.7414.557 [doi]
- International Telecommunication Union. (2013). The world in 2013: The facts and figures. Retrieved from http://www.itu.int/en/ITUD/Statistics/Pages/facts/default.aspx
- Kebaya, L., Nduati, R., Wamalwa, D., Kariuki, N., & Bashir, A. (2014). PO-0260a
 Efficacy of mobile phone use on adherence to nevirapine prophylaxis and retention in care among the hiv-exposed infants in pmtct: A randomised controlled trial.
 Archives of Disease in Childhood, 99(Suppl 2), A329-A329.
 doi:10.1136/archdischild-2014-307384.911

- Kliner, M., Knight, A., Mamvura, C., Wright, J., & Walley, J. (2013). Using no-cost mobile phone reminders to improve attendance for HIV test results: A pilot study in rural swaziland. *Infectious Diseases of Poverty, 2*(1), 12-9957-2-12. doi:10.1186/2049-9957-2-12; 10.1186/2049-9957-2-12
- Kunutsor, S., Walley, J., Katabira, E., Muchuro, S., Balidawa, H., Namagala, E., & Ikoona, E. (2010). Using mobile phones to improve clinic attendance amongst an antiretroviral treatment cohort in rural uganda: A cross-sectional and prospective study. *AIDS and Behavior*, 14(6), 1347-1352. doi:10.1007/s10461-010-9780-2; 10.1007/s10461-010-9780-2
- Lipsey, M., & Wilson, D. (2001). *Practical meta-analysis*. Thousand Oaks, California: Sage publications, Inc.
- Losina, E., Toure, H., Uhler, L. M., Anglaret, X., Paltiel, A. D., Balestre, E., . . . CEPAC International investigators. (2009). Cost-effectiveness of preventing loss to follow-up in HIV treatment programs: A cote d'ivoire appraisal. *PLoS Medicine, 6*(10), e1000173. doi:10.1371/journal.pmed.1000173 [doi]
- Marks, G., Gardner, L. I., Craw, J., & Crepaz, N. (2010). Entry and retention in medical care among HIV-diagnosed persons: A meta-analysis. *AIDS (London, England),* 24(17), 2665-2678. doi:10.1097/QAD.0b013e32833f4b1b [doi]
- McNairy, M. L., Gachuhi, A. B., Lamb, M. R., Nuwagaba-Biribonwoha, H., Burke, S., Ehrenkranz, P., . . . El-Sadr, W. M. (2015). The Link4Health study to evaluate the effectiveness of a combination intervention strategy for linkage to and retention in

- HIV care in swaziland: Protocol for a cluster randomized trial. *Implementation Science : IS, 10,* 101-015-0291-4. doi:10.1186/s13012-015-0291-4 [doi]
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D. G., & PRISMA Group. (2009). Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. PLoS Medicine, 6(7), e1000097. doi:10.1371/journal.pmed.1000097 [doi]
- Mwapasa, V., Pro, G., Chinkhumba, J., Mukaka, M., Kobayashi, E., Stuart, A., . . . Eliya, M. (2014). Mother-infant pair clinic and SMS messaging as innovative strategies for improving access to and retention in eMTCT care and option B+ in malawi: A cluster randomized control trial (the PRIME study). *Journal of Acquired Immune Deficiency Syndromes (1999), 67 Suppl 2*, S120-4.
 doi:10.1097/QAI.000000000000000327 [doi]
- Norton, B. L., Person, A. K., Castillo, C., Pastrana, C., Subramanian, M., & Stout, J. E. (2014). Barriers to using text message appointment reminders in an HIV clinic.

 Telemedicine and E-Health, 20(1), 86-89. doi:10.1089/tmj.2012.0275
- 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; 10.1371/journal.pone.0043832
- 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

- Perron, N. J., Dao, M. D., Kossovsky, M. P., Miserez, V., Chuard, C., Calmy, A., & Gaspoz, J. M. (2010). Reduction of missed appointments at an urban primary care clinic: A randomised controlled study. *BMC Family Practice*, *11*, 79-2296-11-79. doi:10.1186/1471-2296-11-79; 10.1186/1471-2296-11-79
- Reeves, S., Kuper, A., & Hodges, B. D. (2008). Qualitative research methodologies: Ethnography. *BMJ (Clinical Research Ed.)*, 337, a1020. doi:10.1136/bmj.a1020
- Rosen, S., & Fox, M. P. (2011). Retention in HIV care between testing and treatment in sub-saharan africa: A systematic review. *PLoS Medicine*, *8*(7), e1001056. doi:10.1371/journal.pmed.1001056 [doi]
- Schwartz, S. R., Clouse, K., Yende, N., Van Rie, A., Bassett, J., Ratshefola, M., & Pettifor, A. (2015). Acceptability and feasibility of a mobile phone-based case management intervention to retain mothers and infants from an option B+ program in postpartum HIV care. *Maternal and Child Health Journal*, *19*(9), 2029-2037. doi:10.1007/s10995-015-1715-0 [doi]
- Thornton, R. L. (2008). The demand for, and impact of, learning HIV status. *The American Economic Review*, *98*(5), 1829-1863. doi:10.1257/aer.98.5.1829

- UNAIDS. (2012). *Regional fact sheet 2012.* The Joint United Nations Programme on HIV/AIDS (UNAIDS).
- van der Kop, M. L., Ojakaa, D. I., Patel, A., Thabane, L., Kinagwi, K., Ekstrom, A. M., . . . Lester, R. T. (2013). The effect of weekly short message service communication on patient retention in care in the first year after HIV diagnosis: Study protocol for a randomised controlled trial (WelTel retain). *Bmj Open, 3*(6), e003155. doi:10.1136/bmjopen-2013-003155
- WHO. (2014). Global health observatory (GHO), HIV/AIDS: Global situation and trends. (No. 2014). Switzerland, Geneva: World Health Organization (WHO).
- Zou, H., Fairley, C. K., Guy, R., Bilardi, J., Bradshaw, C. S., Garland, S. M., . . . Chen, M. Y. (2013). Automated, computer generated reminders and increased detection of gonorrhoea, chlamydia and syphilis in men who have sex with men. *Plos One*, 8(4), e61972. doi:10.1371/journal.pone.0061972

4 Chapter four: Social capital and retention to care among people living with HIV in Dar es Salaam, Tanzania

4.1 Introduction

Tanzania is among the countries in Africa heavily impacted by the HIV pandemic. Efforts to mitigate the HIV epidemic in Tanzania have reduced HIV prevalence from 7-9% in 2008 to 5.3% in 2012 (Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC), National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), and Macro International Inc., 2008). Meanwhile, youth account for over 60% of new HIV infections. While HIV prevalence is 1.3% among women aged 15 to 19 years, it is 6.3% among women aged 20-24 years. The prevalence among men in these same age groups was 0.7% and 1.7%, respectively. Sixty-five percent of the Tanzanian population is under the age of 24 years. Early sexual debut (13% by age 15 and 59% by age 18 among females), together with inadequate information on HIV, impact the epidemic. HIV remains as a major cause of death and young women of child-bearing years are the most vulnerable (Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC), National Bureau of Statistics (NBS), Office of the Chief Government Statistician (OCGS), and Macro International Inc., 2008).

Social capital is defined as "features and resources -- social norm and trust, for example -- embedded in a social structure which are accessed and/or mobilized in purposive action" (Lin, 1999; Putnam, 2001). People with high social capital have better health outcomes, including higher self-rated health status and lower mortality (Kawachi, Kennedy, & Glass, 1999). Those endowed with social capital experience less barriers

accessing health care and tend to build more trusting relationships with health care providers (Perry, Williams, Wallerstein, & Waitzkin, 2008; Torres, Erwin, Trevino, & Jandorf, 2013). The positive effect of social capital has been consistently demonstrated among people living with HIV (PLWH). PLWH living in a community with high social capital experienced less HIV stigma (Chiu et al., 2008; Sivaram et al., 2009) and women with high social capital have lower HIV incidence over time (Gregson et al., 2011). People with high social capital are more likely to disclose their HIV status and to engage within their social networks, increasing access to resources in the community (Jong & Rankin, 2014).

4.2 Background

Nan Lin's Network Theory of Social Capital articulates how purposive actions to access and mobilize available social capital can yield positive returns for any given inequality. The theory identifies two types of returns: instrumental and expressive. Through instrumental returns, one can expect economic, political, and social returns. Expressive returns can be physical health, mental health, or life satisfaction. Lin explains the mechanism by which embedded resources in social networks yield positive outcomes, using four elements of social capital: information, influence, social credentials, and reinforcement. As individuals strive to maintain social relationships, which provide emotional support and access to certain resources, assurances and recognition from the network reinforce social relationships (Lin, 1999). Figure 4.1 depicts the conceptual framework of this study based on Lin's model.

While relationships between increased social capital and improved health outcomes have been established, significant effects between socioeconomic status

(SES), measured by household income and education level, and health outcomes call into question whether social capital is another proxy for SES. SES then becomes an important concept to explore. SES is known to be an independent predictor of overall health outcomes (Kawachi et al., 1999) and correlates with social capital. Population level studies have found that controlling for SES attenuates the association between social capital and health, but social capital is still an independent and significant predictor of health outcomes (Kawachi et al., 1999; Ziersch, Baum, Macdougall, & Putland, 2005). This study uses the United Nations Development Program (UNDP) multidimensional poverty index (MPI) as a proxy of SES, which provides a comprehensive picture of the level of deprivation based on health, education and living standard (United Nations Development Programe, 2014). MPI is a useful measure of poverty reflecting prevalence and intensity of the poverty experienced by the people in the same community or group. In addition, MPI allows comparing level of poverty across countries and regions internationally (Oxford Poverty and Human Development Initiative, 2014; United Nations Development Programe, 2014). Therefore, a comprehensive assessment of both social capital and poverty will significantly improve the understanding of role these two play on health outcomes.

In the current study, we hypothesized that: 1) PLWH with higher social capital will have better HIV health outcomes compared to PLWH with lower social capital 2) PLWH with higher social capital will be less likely to delay seeking care, will engage in regular medical care, and will have higher immune competency (WHO clinical stages and CD4 cell counts). We also explored the relationship between poverty, using the MPI, and social capital.

4.3 Methods

4.3.1 Study design and sample

We conducted a cross-sectional study in Dar es Salaam, Tanzania between August and September 2015. Inclusion criteria for study participation were adults 18 years or older who spoke English or Swahili, were currently receiving care at six HIV clinics across the city and had an HIV diagnosis confirmed from medical records. We used convenience sampling.

We estimated the sample size required based on a conservative effect size of 0.15 for social capital, to be correlated with good health outcomes measured by mortality (Gilbert, Quinn, Goodman, Butler, & Wallace, 2013). Assuming 5 independent variables and a desired significance level (α) of 0.05 and power (β -1) of 0.80, a sample size of 91 participants was required (Cohen, 1992). Using same parameters but increasing alpha to 0.01, a sample size of 126 participants was required (Cohen, 1992).

4.3.2 Study locations and procedures

Dar es Salaam is the largest city in Tanzania. HIV prevalence in Dar es Salaam is one of the highest in the country (6.9%) (TACAIDS, 2013); The Management and Development for Health (MDH) is non-profit public health organization funded by Health Resources and Services Administration (HRSA), CDC and Harvard University under PEPFAR. MDH provides HIV care services to over 100,000 PLWH in over 50 health facilities in Dar es Salaam and across Tanzania (MDH, 2015). We conducted the study in six care and treatment (CTC) clinics, which provide HIV treatments and also link HIV care between pre-natal care and Prevention of Mother to Child Transmission (PMTCT) programs.

The study had two components for data collection. The first was a questionnaire administered to study participants and the second was a medical chart review.

Research assistants approached patients in the waiting area and recruited them while they were waiting to see their health care providers. Physicians and nurses also referred patients to the research assistants. After receiving written informed consent, trained research assistants either verbally administered the questionnaire in a private room or participants completed the questionnaire on their own. Research assistants then collected additional medical information from patients' medical charts on the same day.

4.3.3 Variables and measures

Independent variables were social capital, demographic characteristics, reasons seeking HIV care, barriers to accessing HIV care, and the multidimensional poverty index (MPI). Social capital was the major independent variables of interest. Dependent variables were initial CD4 cell counts, WHO HIV stage, self-reported health outcomes and retention in care. Two independent bilingual research assistants conducted translation of the questionnaire and consent to Swahili and back-translation to English. We piloted the questionnaire and consent with research assistants and three women who were eligible for participation.

Social capital: We used the marginalization and social capital scale by Bullen and Onyx (Onyx & Bullen, 2000). Validity and reliability of the instrument based on an Australian population was 0.84 (Cronbach's alpha coefficient) (Onyx & Bullen, 2000). The instrument was also used among PLWH in a large international, multicenter research study (Cronbach's alpha coefficient = 0.88) (Webel et al., 2012). This

instrument encompasses eight dimensions of social capital: participation in the local community (7 items), social agency (7 items), feelings of trust and safety (5 items), neighborhood connections (5 items), friends and family connections (3 items), tolerance of diversity (2 items), value of life (2 items), and workplace connections (3 items). Each item is calculated based on a 4-point Likert scale ranging from 1=not much to 4=very much, with a range of 0 to 136 for the total scale. The total mean score is used to interpret the level of social capital. As a categorical variable, 1 is equal to very low on social capital and 4 is high social capital (Onyx & Bullen, 2000). This scale can be analyzed as a continuous variable.

Reasons seeking care and HIV disclosure: Several significant factors for failure to seeking HIV care for women include: not having access to HIV care, not having a known HIV-positive family member, and not having disclosed HIV status (Nguyen, Bygbjerg, Mogensen, & Rasch, 2010; Stein et al., 2000). Women who have competing caregiver responsibilities delay seeking HIV care (Stein et al., 2000). Other factors associated with delays in health seeking behaviors are knowledge and health literacy, economic status and access to care, fear and stigma, health status and health perception, substance use and mental health, and readiness to receive care (Health Resources and Services Administration, HIV/AIDS Bureau, 2006). The reasons and motivation for seeking care may be explained by how patients view and use their resources and support. Therefore, we developed two multiple choice research questions (What encouraged you to get tested for HIV? and What prevented you from coming to HIV clinic or hospital to get care after you found out your HIV status?) in the questionnaire accessing encouraging and preventing factors of seeking HIV care.

Multidimensional poverty index (MPI): We measured economic status by asking about their perceived income adequacy, -whether their income was enough to maintain their daily life and it has been used to assist with resource allocation for both policy development and program implementation (Oxford Poverty and Human Development Initiative, 2014). However, household income is a poor measure of poverty in many countries. The United Nations Development Program (UNDP) introduced the MPI in 2010(United Nations Development Programe, 2014). The MPI is comprised of ten weighted questions measuring 3 dimensions of poverty—health, education and living standard, and is used to evaluate household level poverty and deprivation in each dimension (Oxford Poverty and Human Development Initiative, 2014). This each dimension is given one-third weight of the total score. MPI is the product of 'incidence (H)' and 'intensity (A)' of poverty (MPI=HxA). Incidence is the percentage of people who are poor and intensity is the average share of 10 indicators where poor people are impoverished (Oxford Poverty and Human Development Initiative (OPHI), 2015a). MPI measures individual level of poverty based on the household deprivation score; the poverty cut-off point for Tanzania is 33.3%. In other words, individuals in a household with an MPI score 33.3% or higher are considered to be poor.

There are two indicators in health dimension: child mortality in the last five years and malnourishment for any child and adult. The two indicators in education are: years of schooling (no household member completing five years of schooling indicating poverty) and child school attendance for any school-aged child up to primary education. Living standard has six indicators: access to electricity, sanitation (separate latrine, not shared with other households), safe drinking water, and flooring (dirt, sand, or dung floor

indicating poverty). In addition, use of dung, wood or charcoal as cooking fuel and household ownership of the following items (radio, TV, telephone, bike, motorbike, refrigerator, and a car) assess living standard.

Initial CD4 cell counts and WHO HIV stage: CD4 T-cell count is an important parameter in HIV care and is used to assess patients' immune competency and guides clinical management such as disease staging. The normal CD4 cell count ranges between 800 to 1050 cells/mm³. A CD4 count less than 200 cells/mm³ suggests progression to AIDS (Bartlett, 2012). Tanzania follows the World Health Organization (WHO) guidelines to treat HIV and provides ART for those with CD4 cell counts less than 350 cells/mm³ (National AIDS Control Programme (NACP), 2009; World Health Organization, 2007). As an indicator for disease progression and patients' immune competency when engaging to care, we extracted documented CD4 cell counts prior to starting ART from medical records. If CD4 T-cell count was not available, the WHO HIV staging system was substituted. This staging is an important clinical parameter for HIV treatment in resource-limited settings. Staging can guide initiation of ART along with CD4 counts. There are 4 categories from stage 1 (asymptomatic HIV infection), stage 2 (moderate unexplained weight loss (<10% of presumed or measured body weight) and recurrent opportunistic infections) to stage 3 and stage 4. Progression to stage 3 and 4 requires ART regardless CD4 cell counts (National AIDS Control Programme (NACP), 2009; World Health Organization, 2007). The stages were made by health care providers at the clinics and extracted from medical records.

<u>Self-reported health outcomes: Quality of Life (QoL) –SF12</u>: This study used the Short Form (SF-12) of Medical Outcome Survey (MOS-HIV), which evaluates

comprehensive health status pertaining to HIV and AIDS. SF-12 is a shorter version of MOS-HIV with 12 items measuring 8 domains of health: energy/fatigue, pain, physical, social, role, and emotional functioning, mental health and general health, which cluster into two factors: physical and mental health score (Han, Pulling, Telke, Huppler Hullsiek, & Terry Beirn Community Programs for Clinical Research on AIDS, 2002). The composite scores, derived from twelve questions range from 0 to 100; higher scores indicate better quality of life in relation to health status. As one of the most frequently used health related quality of life measure, this measure is known to be valid and reliable in many settings, and patient populations, not limited to PLWH (Han et al., 2002). We used a validated Swahili version of SF-12 (Wagner et al., 1999).

Retention to care: We measured retention to care based on clinic non-attendance, defined as 'patients did not return to appointment within four weeks from the date of follow-up appointment given by health care providers'. For example, if a patient showed up 5 days before (or after) the appointment, it was counted as attendance. The number of appointments made with patients and the number of attended visits within the defined time frame were obtained from medical charts, allowing us to calculate attendance rate, in other words, retention to care.

4.4 Analysis

We conducted descriptive statistical analysis of each variable (mean, SD, range, proportion) and t-test by gender assuming non-equal variance between the groups (Harris et al., 2009; StataCorp, 2013). Bivariate correlation analysis was conducted between variables using Pearson and Spearman's correlation for normally distributed and non-normally distributed variables, respectively (Table 4.4) to determine directions

and magnitude of association among variables. To test the research hypothesis-social capital predicts HIV health outcome, we used bivariate analysis of variables against high and low social capital (cutoff point of 2.5) and included variables that were significant at p value less than 0.05 in a multiple linear regression analysis as well as selected covariates based on the conceptual framework informed by 'network theory of social capital' (Lin, 2000). We tested interaction terms (social capital and gender) in the models. After fitting the full model with all the variables, we kept covariates, that were significantly related (p<0.05) to the HIV health outcome. We used bootstrapping method to correct non-normality of the sampling distribution of dependent variable, HIV health outcome (skewness=-.94) (Vittinghoff, Glidden, Shiboski, & McCulloch, 2005).

Questionnaires were entered and managed using REDCap electronic data capture tools hosted at University of California, San Francisco and analyzed in Stata version 13 (Harris et al., 2009; StataCorp, 2013).

4.4.1 Ethical approval and consent process

This study was approved by the Institutional Review Board (IRB) of University of California, San Francisco (UCSF) and Muhimbili University of Health and Allied Sciences (MUHAS) in 2015. Health care providers informed the patients about the study at the HIV clinics. Research assistants obtained written informed consent from patients in a private room before conducting the questionnaires.

4.5 Results

4.5.1 Demographic characteristics

Table 4.1 shows demographic characteristics of the 163 participants recruited from six MDH CTC clinics. Average age of the sample was 41 years old and ranged between 19

to 77 years old. The majority of the participants were women (76%) with an average age of 39.6 years (SD=9.5), which was younger than male participants (43.6 years, SD=10.6). About 70% reported that they did not work for pay and 15% said their household income was enough to cover daily expenses. Also, 80% had 7 years of primary education or less (Table 4.1).

4.5.2 HIV biomarkers

All participants had HIV confirmed by medical record. The average time since diagnosis with HIV was 3.8 years (standard deviation=2.52). The Tanzanian national guideline for HIV management recommends that ART be started when CD4 cell counts are less than 350 or patient is WHO clinical stage 3 or 4. In this sample, Over 90% were on anti-retroviral therapy (ART). Mean naïve CD4 counts prior to starting ART was 276.9 cells/mm³ (SD=235.2, range 3 to 1441) (Table 4.1). Over 60% joined HIV care with WHO stage 3 or 4 and 74% had initial CD4 cell counts less than 350 (n=143). Over 90% were on anti-retroviral therapy (ART).

4.5.3 HIV care seeking behavior

Voluntary counseling and testing for HIV was the primary manner that participants received their HIV diagnosis (64.8%) followed by health care provider initiated HIV testing at a hospital or clinic (32.7%). Twenty-eight participants (17.2%) responded that they were diagnosed during prenatal care or childbirth.

The motivation to seek an HIV test was mainly based on frequent illnesses (59.5%) or having a partner with HIV (9.8%). The majority of participants reported no barriers to accessing HIV care after diagnosis (95%). Other barriers were stigma associated with HIV (5 respondents), no reason to seek medical care because they

were feeling fine (3 respondents), too sick to come to hospital or clinic (3 respondents), and lack of transportation to care (3 respondents), and lack of knowledge to access to care (2 respondents). We also asked questions in order to understand acceptability of community dispensary for ART when access to care becomes a barrier. Almost 10% of the participants had someone else collect their ART and collected ART for others.

4.5.4 Multidimensional Poverty Index (MPI)

A higher MPI score means a participant is multidimensionally deprived in health, education, or household assets. Thirty-nine participants (24%, incidence of poverty (H)) were living in poverty and intensity of the poverty among the poor was 40 percent (A) (Table 4.1). Across all study participants, PLWH from six HIV clinics, the MPI score was 0.09 (HxA), which is lower than Tanzanian national level of 0.33, and is also lower than Tanzanian urban average of 0.15 (Oxford Poverty and Human Development Initiative (OPHI), 2015b). Most of the participants had access to a separate latrine and food, as measured by low level of malnourishment among children living in the home. The proportion of having had a child die in the home was high among the poor. All of the poor used charcoal as a cooking fuel (Figure 4.2).

While the MPI identified 24% of the participants were multidimensionally poor, 85% of the participants reported their income was either barely adequate (47.2%) or totally inadequate (37.4%) (Table 4.1). The two measures, MPI and income adequacy were not correlated (Spearman rho=0.13, p=0.1).

4.5.5 Retention in care

Overall, participants had high retention to care. Seventy-seven (47.2%) participants had never missed their follow-up HIV care appointments in the past 5 years.

The number of missed visits per year was 0.59 and the retention rate was 92.7% (Table 4.2).

4.5.6 Social Capital

The mean social capital score was 2.61 (SD= 0.45). This score is slightly higher than the cut-off point of 2.5, low and high social capital (Díaz, Drumm, Ramírez-Johnson, & Oidjarv, 2002). Webel and colleagues reported social capital score of 2.68 (SD=0.55) from an international studies including 1,963 PLWH from five countries, which was slightly higher than our study results (2012).

For hypothesis 2, we did not find any significant associations between the positive effects of social capital on HIV related health outcomes (retention to care, immune competency) (Table 4.4). However, there was a significant effect for gender t(69.4) = -2.46, p<0.05); males had higher social capital scores than females (Table 4.3). We also explored the relationship between poverty, using the MPI, and social capital. There was a significant effect for poverty, t(77.28)= 2.08, p<0.05); participants who were impoverished had lower social capital (n=42, mean=2.48, SD=0.43) than those who were not in poverty (n=121, mean=2.65, SD=0.47).

4.5.7 Health related quality of life (QoL)

QoL score was 42.91 (SD=5.56) among the participants. Mental and physical health are two factors comprising QoL. Mental health score (41.15, SD=9.75) was significantly lower than physical health score (45.78, SD=6.10) among the participants, t(316)=5.08), p<0.01. Males (44.7, SD=4.2) had a significant higher scores compared to females (42.3, SD=5.8), t(88.09)= -2.87, p<0.01 (Table 4.3). There was no gender difference in

physical health however; females had significantly lower mental health scores (40.01, SD=10.28) than males (44.66, SD=6.87), t(97.0)= -3.22, p<0.01.

4.5.8 Multiple linear regression model predicting HIV health outcomes
In a bivariate correlation (Table 4.5), increased social capital had a weak but statistically significant association with improved health status (r=0.23). Social capital correlated with poverty, based on the MPI, and age, measured in years, and their relationships were weak; the poorer had lower social capital (r=-0.17) and the older had the higher social capital (r=0.18). WHO HIV stage is primarily used when biomarkers such as CD4 counts is not available to assess progression of HIV; the CD4 cell counts (n=149) and WHO HIV stage (n=157) showed an inverse, weak association (rho=-0.283). Older age was significantly associated with higher WHO HIV stage upon diagnosis (rho=0.284). Lastly, PLWH who stayed in care for longer time, as measured by years since HIV diagnosis, were more likely to have missed appointments (r=-0.237).

Social capital and gender were the only significant predictors of QoL based on bivariate analysis (p-value at 0.05). We also included variables into the model if they had significant associations with social capital, our primary research interest. Lastly, retention rate to HIV care was entered to the model based on our conceptual framework. Therefore social capital, gender, age, poverty and retention rate were entered to a multiple linear regression model, with QoL as the outcome variable of interest.

Both social capital and gender were significantly associated with health outcomes measured by QoL among our sample of PLWH in an urban area of Tanzania (Table 4.5). Because the level of social capital and QoL differed by gender, we

assessed the interaction between social capital and gender in our multivariate model. This interaction was not statistically significant (p=0.46), and was thus excluded from the final model. PLWH with more social capital had better health outcomes (beta coefficient=2.47, 95% Cl=0.73, 4.19) after conditioning on gender, age, poverty, and retention to care. Males reported better health status compared to females (beta coefficient=2.14, 95% Cl=0.51, 3.78) after conditioning on social capital, age, poverty, and retention to care. This model explained about 7 percent of the variance in self-reported health related QoL (Table 4.5).

4.6 Discussion

In a sample of 163 PLWH in Dar es Salaam, Tanzania, we found that social capital was an independent determinant of self-reported health outcomes. While poverty correlated with social capital, poverty was not associated with self-reported health, or with measured CD4 cell counts or WHO HIV stage. This study reinforces the importance of social capital on health-related QoL; PLWH with higher social capital are inclined to report significantly better health outcomes. This result is consistent with previous study findings (Kawachi et al., 1999; Webel et al., 2012) and strengthens the importance of social capital in relation to health among socially marginalized people with HIV in Tanzania.

We observed a differential impact on QoL based on gender among PLWH in this sample. Women had poorer health status compared to men after adjusting for social capital. Lin explains that inequality of social capital based on gender is due to differences in social networks that each group has accesses to, particularly, the extent of resources in the network. Social capital and network typically decreases for women

rearing children. Women's networks tend to extend to relatives and neighbors, while men maintain wider community and work networks, which is more likely to increase social capital (Lin, 2000).

While the role of gender in social capital has mixed outcomes across health outcomes in different societies, men consistently report higher social capital compared to women (Eriksson, Ng, Weinehall, & Emmelin, 2011; Vyncke et al., 2014). However, women may benefit more from social capital than men. Eriksson et al. analyzed population level of data in Sweden and found an association between social capital and self-rated health only among women, but not men (Eriksson et al., 2011). Vyncke et al. emphasized greater importance of social capital for women particularly those living in vulnerable and deprived situations (Vyncke et al., 2014).

In the present study, women had very high adherence to care. However, they had minimal education and many lived in poverty. They learned about their HIV status during prenatal care. Although our study did not detect an interaction between gender and social capital, a mediation effect of gender on the relationship between social capital and health needs to be further evaluated in larger studies in resource limited settings.

Our study affirms the independent role of social capital in self-reported health outcomes, which is consistent with other studies (Kawachi et al., 1999; Ziersch et al., 2005). We used multidimensional poverty index (MPI) as a proxy for SES and found a significant correlation with social capital, but which was not associated with health outcomes. MPI was based on actual items and standards that households' access to clean water, sanitation, and history of child death rather than participants' perceived

income adequacy. And this could be because the MPI does not capture the positive effect of possessing higher SES, represented by household income (Kawachi et al., 1999).

This study has several limitations. First, the study design was cross-sectional, which limits inference about a causal relationship between social capital and self-reported health outcomes in this sample. Second, we recruited participants using a convenience sample design in six clinics where women were already receiving care for HIV. Therefore, the study results may not apply to other settings. Third, PLWH's retention to care was our research interest and we found fairly high adherence to care appointment. As we included PLWH who already presented to the appointment, sampling bias is a limitation of our study to assess retention rate and lost to follow up.

The President's Emergency Plan for AIDS Relief (PEPFAR) recently reported that up to two-thirds of patients in developing countries may be lost to follow-up after HIV diagnosis and before starting ART (Rosen & Fox, 2011). Being lost to follow-up (LTFU) is a significant predictor of progression of HIV disease (Berg et al., 2005). Non-adherence to medications among those LTFU leads to further worsening of HIV disease, posing a higher risk of HIV transmission to others in the community (Berg et al., 2005; Gardner, McLees, Steiner, Del Rio, & Burman, 2011). Therefore, patient retention has been a central challenge in the provision of HIV care, not only because of patient care costs and constraints on health care resources, but also because of poor health outcomes associated with missed or lost follow-up appointments. Due to our study limitations, we were not able to find any significant predictors of LTFU, therefore we encourage further studies to include PLWH outside of clinical care.

4.7 Conclusion

Our study examined several variables in relation to HIV care outcomes in urban HIV clinics in resource-limited country. Although causal inference cannot be drawn between improved social capital and improved self-reported health outcome in our study, the results warrant future studies to explore the complex relationships and to intervene on programs that improve social capital among PLWH. HIV disproportionately affects young women in Tanzania. These women can benefit from having formal and informal social networks that build social capital, leading to improved quality of life while managing a chronic disease like HIV.

Table 4.1 Characteristics of study participants

Variable	N= 163			
Age, years, mean (SD, range)	40.6 years (9.9, 19-77)			
Sex, n (%)				
Male	39 (23.9)			
Female	124 (76.1)			
Work for pay, n (%)				
Yes	49 (30.1)			
No	114 (69.9)			
Income, n (%)				
Totally inadequate	61 (37.4)			
Barely adequate	77 (47.2)			
Enough	25 (15.3)			
Education, n (%)				
None	3 (1.8)			
Primary school	127 (77.9)			
Secondary school	24 (14.7)			
High school	5 (3.1)			
Collage or higher	4 (2.5)			
Individual deprivation score (Poverty) ¹	2.05 (1.53, 0-8.37)			
Multidimensional Poverty Index $(MPI)^2 = (HxA)$	0.09			
Incidence of Poverty (H) ³	23.5%			
Average Intensity across the poor (A) ⁴	39.9%			
Initial CD4 count (cells/mm³), mean (SD, range)	276.85 (235.16, 3-1441)			
Number of people with CD4 count less than 350	110 out of 149 ⁵ (73.8%)			
cells/mm ³ , n (%)				
WHO HIV stage, n (%)				
Stage 1	40 (25.5%)			
Stage 2	22 (14.0%)			
Stage 3	81 (51.6%)			
Stage 4	14 (8.9%)			
On antiretroviral, n (%)	149 (91.4)			
Years with HIV, mean (SD, range)	3.8 (2.52, 0.1-11.3)			

Poverty scores higher than 3.33 are considered being deprived and range between 0 and 10 MPI reflects poverty level among the study participants

Percentage of people who are poor

Average share of poverty indicators where poor people are impoverished Naïve CD4 counts were available for 149 participants due to pending results (n=8) or data not available (n=6)

Table 4.2 Retention to care among PLWH at 6 HIV clinics in Dar es Salaam, Tanzania

Retention measure					
Missed visits (count/year), mean (SD, range)	0.50 (4.00, 0.5.67)				
Number of missed visits/scheduled visits in past 12 months	0.59 (1.02, 0-5.67)				
Retention rate, percent (SD, range)	00.70/ (44.400)				
Proportion of kept visits out of scheduled	92.7% (44-100)				

Table 4.3 Quality of life and social capital by gender

Variables	Mean (SD) (n=163)	Female (n=124)	Male (n=39)	t ¹ (df ²)	Significance (p-value)
Social Capital	2.61 (0.45)	2.56 (0.07)	2.75 (0.04)	-2.46 (69.37)	0.02
Quality of Life	42.91 (5.56)	42.3 (5.8)	44.7 (4.2)	-2.87 (88.09)	0.005

¹T-test: unequal variance assumed ²Satterthwaite's degrees of freedom

Table 4.4 Bivariate correlations (Pearson¹ or Spearman's² correlation) among the variables

Variables	Social Capital	Quality of life	Poverty	CD4 cell counts	WHO HIV stages	Retention rate	Age	HIV years	Gender
Social Capital	1								
Quality of life	0.234*	1							
Poverty ³	-0.169*	-0.112	1						
CD4 cell counts	-0.054	0.039	0.051	1					
WHO HIV stages	0.069	-0.008	-0.048	-0.283*	1				
Retention rate ⁴	-0.118	-0.008	0.083	-0.077	0.027	1			
Age, years	0.180*	0.118	0.073	-0.086	0.284*	-0.012	1		
HIV years	0.092	0.095	0.113	-0.077	0.046	-0.237*	0.113	1	
Female	-0.180*	-0.192*	0.127	-0.026	-0.119	-0.119	-0.177*	0.911	1

Normally distributed variables used Pearson's correlation
 Non-normally distributed variables used Speaman's rank correlation
 Individual deprivation score based on 10 poverty indicators
 Proportion of kept clinic appointment out of scheduled

Table 4.5 Multiple linear regression model predicting Quality of life (QoL)¹ among PLWH in Tanzania (N=163)

Predictors ²	Beta coefficient	Bootstrap standard error	Z-score	P value	95% confidence interval	
Social capital ³	2.47	0.88	2.79	0.005	0.73, 4.19	
Male	2.14	0.83	2.57	0.010	0.51, 3.78	
Age	0.02	0.05	0.35	0.723	-0.07, 0.10	
Poverty ⁴	-0.28	0.33	-0.85	0.398	-0.93, 0.37	
Retention to care ⁵	-0.01	0.03	-0.16	0.875	-0.07, 0.06	

Model $R^2 = 0.10$; adjusted $R^2 = 0.07$

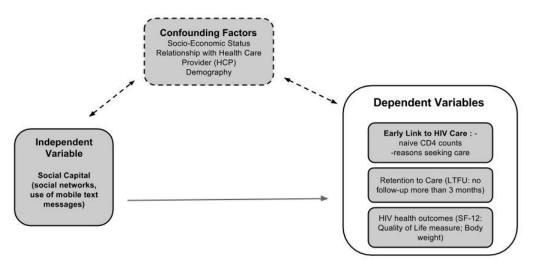
Health related QoL measured by SF-12

Predictors are centered at zero center mean

Social capital measured by 'Measurement of Social Capital' by Bullen and Onyx (2012)

Individual deprivation score based on 10 poverty indicators

Proportion of kept clinic appointment out of scheduled



<Conceptual & Analytical Framework of the Study>

Figure 4.1 Conceptual framework of the study

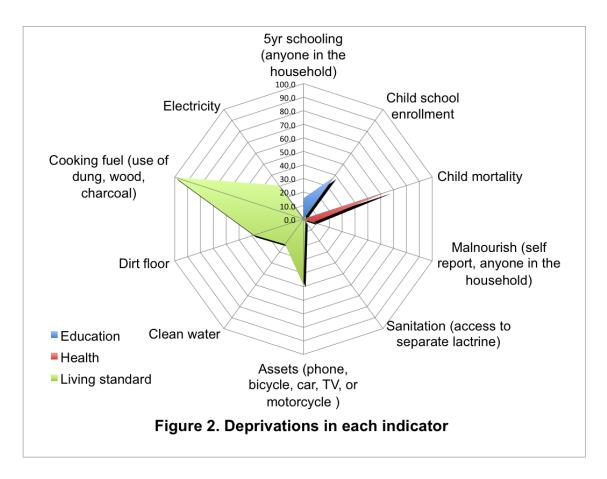


Figure 4.2 Deprivations in each indicator

References

- Bartlett, J. (2012). **Techniques and interpretation of measurement of the CD4 cell count in HIV-infected patients**. Retrieved from http://www-uptodatecom.ucsf.idm.oclc.org/contents/techniques-and-interpretation-of-measurement-ofthe-cd4-cell-count-in-hiv-infectedpatients?source=search_result&search=cd4+count&selectedTitle=1%7E150
- Berg, M. B., Safren, S. A., Mimiaga, M. J., Grasso, C., Boswell, S., & Mayer, K. H. (2005). Nonadherence to medical appointments is associated with increased plasma HIV RNA and decreased CD4 cell counts in a community-based HIV primary care clinic. *AIDS Care*, *17*(7), 902-907. doi:W74171324K2312M1 [pii]
- Chiu, J., Grobbelaar, J., Sikkema, K., Vandormoel, A., Bomela, N., & Kershaw, T. (2008). HIV-related stigma and social capital in south africa. AIDS Education and Prevention: Official Publication of the International Society for AIDS Education, 20(6), 519-530. doi:10.1521/aeap.2008.20.6.519; 10.1521/aeap.2008.20.6.519
- Cohen, J. (1992). A power primer. Psychological Bulletin, 112(1), 155-159.
- Díaz, H. L., Drumm, R. D., Ramírez-Johnson, J., & Oidjarv, H. (2002). Social capital, economic development and food security in peru's mountain region. *International Social Work, 45*(4), 481-495. doi:10.1177/00208728020450040601
- Eriksson, M., Ng, N., Weinehall, L., & Emmelin, M. (2011). The importance of gender and conceptualization for understanding the association between collective social

- capital and health: A multilevel analysis from northern sweden. *Social Science* & *Medicine* (1982), 73(2), 264-273. doi:10.1016/j.socscimed.2011.05.013 [doi]
- Gardner, E. M., McLees, M. P., Steiner, J. F., Del Rio, C., & Burman, W. J. (2011). The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. *Clinical Infectious Diseases : An Official Publication of the Infectious Diseases Society of America*, 52(6), 793-800.
 doi:10.1093/cid/ciq243 [doi]
- Gilbert, K. L., Quinn, S. C., Goodman, R. M., Butler, J., & Wallace, J. (2013). A metaanalysis of social capital and health: A case for needed research. *Journal of Health Psychology, 18*(11), 1385-1399. doi:10.1177/1359105311435983 [doi]
- Gregson, S., Mushati, P., Grusin, H., Nhamo, M., Schumacher, C., Skovdal, M., . . .

 Campbell, C. (2011). Social capital and women's reduced vulnerability to HIV infection in rural zimbabwe. *Population and Development Review*, *37*(2), 333-359.
- Han, C., Pulling, C. C., Telke, S. E., Huppler Hullsiek, K., & Terry Beirn Community Programs for Clinical Research on AIDS. (2002). Assessing the utility of five domains in SF-12 health status questionnaire in an AIDS clinical trial. *AIDS* (London, England), 16(3), 431-439.
- Harris, P. A., Taylor, R., Thielke, R., Payne, J., Gonzalez, N., & Conde, J. G. (2009).

 Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of Biomedical Informatics*, *42*(2), 377-381. doi:10.1016/j.jbi.2008.08.010 [doi]

- Health Resources and Services Administration, HIV/AIDS Bureau. (2006). Engaging people in HIV care: Summary of a HRSA/HAB 2005 consultation on linking PLWH into care. ().Health Resources and Services Administration.
- Jong, S., & Rankin, S. (2014). Social capital, faith-based organizations, and malawi persons living with HIV (PLWH). *Annals of Global Health, 80*(3), 196-197. doi:10.1016/j.aogh.2014.08.074
- Kawachi, I., Kennedy, B. P., & Glass, R. (1999). Social capital and self-rated health: A contextual analysis. *American Journal of Public Health*, 89(8), 1187-1193.
- Lin, N. (1999). Building a network theory of social capital. *Connections*, 22(1), 28-51.
- Lin, N. (2000). Inequality in social capital. *Contemporary Sociology*, 29(6), 785-795.
- MDH. (2015). Management and development for health. Retrieved from http://mdhtz.org
- National AIDS Control Programme (NACP). (2009). *Natioinal guidelines for the management of HIV and AIDS*. (No. 3rd edition). Tanzania: Government of Tanzania.
- Nguyen, N. T., Bygbjerg, I. C., Mogensen, H. O., & Rasch, V. (2010). Factors associated with the failure to seek HIV care and treatment among HIV-positive women in a northern province of vietnam. *AIDS Patient Care and STDs*, *24*(5), 325-332. doi:10.1089/apc.2009.0285 [doi]

- Onyx, J., & Bullen, P. (2000). Measuring social capital in five communities. *The Journal of Applied Behavioral Science*, *36*(1), 23-42. doi:10.1177/0021886300361002
- Oxford Poverty and Human Development Initiative. (2014). Global multidimentional poverty index. Retrieved from http://www.ophi.org.uk/multidimensional-poverty-index/
- Oxford Poverty and Human Development Initiative (OPHI). (2015a). Global multidimensional poverty index 2015. Retrieved from http://www.ophi.org.uk/wp-content/uploads/Global-MPI-8-pager_10_15.pdf
- Oxford Poverty and Human Development Initiative (OPHI). (2015b). OPHI country briefing dec 2015: Tanzania. Retrieved from http://www.dataforall.org/dashboard/ophi/index.php/mpi/country_briefings
- Perry, M., Williams, R. L., Wallerstein, N., & Waitzkin, H. (2008). Social capital and health care experiences among low-income individuals. *American Journal of Public Health*, *98*(2), 330-336. doi:10.2105/AJPH.2006.086306 [doi]
- Putnam, R. D. (2001). Social capital: Measurement and consequences. *Isuma:*Canadian Journal of Policy Research, 2
- Rosen, S., & Fox, M. P. (2011). Retention in HIV care between testing and treatment in sub-saharan africa: A systematic review. *PLoS Medicine*, *8*(7), e1001056. doi:10.1371/journal.pmed.1001056 [doi]

- Sivaram, S., Zelaya, C., Srikrishnan, A. K., Latkin, C., Go, V. F., Solomon, S., & Celentano, D. (2009). Associations between social capital and HIV stigma in chennai, india: Considerations for prevention intervention design. AIDS Education and Prevention: Official Publication of the International Society for AIDS Education, 21(3), 233-250. doi:10.1521/aeap.2009.21.3.233; 10.1521/aeap.2009.21.3.233
- StataCorp. (2013). *Stata statistical software* (Release 13 ed.). TX: College Station: StataCorp LP.
- Stein, M. D., Crystal, S., Cunningham, W. E., Ananthanarayanan, A., Andersen, R. M., Turner, B. J., . . . Schuster, M. A. (2000). Delays in seeking HIV care due to competing caregiver responsibilities. *American Journal of Public Health, 90*(7), 1138-1140.
- Tanzania Commission for AIDS (TACAIDS), Zanzibar AIDS Commission (ZAC),
 National Bureau of Statistics (NBS), Office of the Chief Government Statistician
 (OCGS), and Macro International Inc. (2008). *Tanzania HIV/AIDS and malaria indicator survey 2007-2008.* (). Dar es Salaam, Tanzania: TACAIDS, ZAC, NBC,
 OCGS, and Macro International Inc.
- Torres, E., Erwin, D. O., Trevino, M., & Jandorf, L. (2013). Understanding factors influencing latina women's screening behavior: A qualitative approach. *Health Education Research*, *28*(5), 772-783. doi:10.1093/her/cys106 [doi]
- United Nations Development Programe. (2014). Multidimentional poverty index (MPI).

 Retrieved from http://hdr.undp.org/en/content/multidimensional-poverty-index-mpi

- Vittinghoff, E., Glidden, D. V., Shiboski, S. C., & McCulloch, C. E. (2005). Mediation.

 Regression methods in biostatistics: Linear, logistic, survival, and repeated

 measures models (1st ed., pp. 95) Springer.
- Vyncke, V., Hardyns, W., Peersman, W., Pauwels, L., Groenewegen, P., & Willems, S. (2014). How equal is the relationship between individual social capital and psychological distress? A gendered analysis using cross-sectional data from ghent (belgium). *BMC Public Health*, 14, 960-2458-14-960. doi:10.1186/1471-2458-14-960 [doi]
- Wagner, A. K., Wyss, K., Gandek, B., Kilima, P. M., Lorenz, S., & Whiting, D. (1999). A kiswahili version of the SF-36 health survey for use in tanzania: Translation and tests of scaling assumptions. *Quality of Life Research : An International Journal of Quality of Life Aspects of Treatment, Care and Rehabilitation, 8*(1-2), 101-110.
- Webel, A., Phillips, J. C., Rose, C. D., Holzemer, W. L., Chen, W. T., Tyer-Viola, L., . . . Salata, R. A. (2012). A cross-sectional description of social capital in an international sample of persons living with HIV/AIDS (PLWH). *BMC Public Health,* 12, 188-2458-12-188. doi:10.1186/1471-2458-12-188; 10.1186/1471-2458-12-188
- World Health Organization. (2007). WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.

Ziersch, A. M., Baum, F. E., Macdougall, C., & Putland, C. (2005). Neighbourhood life and social capital: The implications for health. *Social Science & Medicine (1982),* 60(1), 71-86. doi:10.1016/j.socscimed.2004.04.027

5 Chapter Five: Discussion and Conclusion

This dissertation aims to deepen understanding of the concept of 'social capital' as one of the seminal social determinants of health(National Institutes of Health, 2001). The importance of social capital on the attainment of better health has been well studied over the past several decades, and this dissertation seeks to deepen the understanding of the role of social capital among PLWH in the context of global health. More specifically, this dissertation scrutinizes the complexity of the concept of social capital to find out which aspects of the concept play a major role in relation to better health outcomes (chapter 2) and reviews application of the concept in clinical practice (chapter 3). Then, chapter 4 employs social capital framework in a resource limited, clinical setting to replicate previous research findings among PLWH and to inform future studies.

This final chapter of the dissertation will highlight each chapter's research findings and then will review overall contributions to social-behavioral research.

Limitations of the research will be discussed together with implications for future studies.

5. 1 Chapter 2

The second chapter examined the relationships between social capital and HIV health outcomes and found that having a higher level of social capital was associated with better self-reported health outcomes among PLWH in the United States. PLWH endowed with social capital were more likely to build trusting relationships with their health care providers (HCP). The relationship was partially mediated by PLWH's engagement with HCP.

Chapter 2 focused on diverse attributes of social capital. The study hypothesis, that only certain dimensions of the concept will convey positive effects of social capital

on health, was tested. Social capital among PLWH in the United States was comprised of three factors: social connection, community participation, and tolerance toward diversity. Social connection played the major role in improving health outcomes followed by tolerance diversity. Social connection is an aspect of social capital encompassing a range of supportive and resourceful social networks: family, friends, and neighbors in a given community. Interestingly, community participation was not a significant factor of social capital in relation to improved HIV health outcomes, which differed from findings from previous research.

Community participation has known to be an essential aspect of having higher social capital. Active community participation links people to opportunities and resources to attain and maintain their social capital. People with high social capital are more likely to participate in community activities. However, the first chapter study did not find this association among the PLWH. Their health status with chronic illnesses and experience of stigma associated with HIV may prevent PLWH from active community participation.

5.2 Chapter 3

The third chapter of the dissertation is a systematic meta-analysis examining efficacy of mobile phone reminders on improving HIV patients' return to care. Nine studies, including five randomized controlled trials (RCT), from seven countries yielding to heterogeneity of the analysis. PLWH who received mobile phone reminders for their follow-up appointments were two times more likely to return to the care than those who didn't receive reminders; however, this estimate was not statistically significant (pooled odd ratio (OR) =2.04, 95% CI: 0.97-4.27). Sensitivity analysis was conducted based on

study designs, sample characteristics, and countries/regions and meta-analysis of five RCTs showed a strong efficacy of the mobile phone reminder (OR =2.04, 95% CI: 1.11-3.74). Studies targeting mothers (and babies who were exposed to HIV during pregnancy and birth) showed that mobile phone reminders was an effective measure to improve retention to care among women with HIV in resource poor settings. Women who received mobile phone reminders were three times more likely to bring their babies for HIV testing and follow-ups (OR=2.92, 95% CI: 1.13-7.53).

This study approaches mobile phone reminders not only as technological innovation but as a tool to improve social capital among a vulnerable population. This study reinforces that mobile phones provide platforms for social capital, allowing information and communication to flow and grow. These new technologies should not merely be used to send reminders in the traditional ways, but should be interactive. Mobile phone reminders have the potential to change PLWH's health related behaviors, including adherence to medical appointments, more effectively.

5.3 Chapter 4

Chapter 4 reports findings from a cross-sectional study of 163 participants in urban HIV clinics in Dar es Salamm, Tanzania. The purpose of the study was to examine the association between social capital and HIV health outcomes, measured by health related quality of life measure. The study found that social capital was an independent predictor of higher quality of life among PLWH in this setting. Women with HIV were likely to have less social capital and report lower quality of life compared to male counterparts. Considering that women of reproductive age are the most vulnerable to HIV infections, and have the highest HIV incidence in resource limited settings, this

study affirms needs for gender specific interventions to strengthen women's social networks and social capital. Age was positively associated with level of social capital, such that as PLWH age, their social networks tend to extend within a given community. This finding is important to reinforce in future intervention studies.

5. 4 Contributions of this dissertation

This study contributes to social-behavioral and nursing research by identifying the importance of social connections over other aspects of social capital such as community participation, norm, trust, and feeling of safety. The known complexity and multi-dimensionality of social capital has been a challenge—where to intervene, and how? Findings from Chapter 1 suggest that social networks to promote health related quality of life among PLWH need to be strengthened. Also, this study found a mediating effect of engagement with health care providers (HCP) between social capital and health related QoL. In particular, the positive effect of having tolerance toward diversity on QoL was solely mediated by engagement with HCP. This is a very useful finding for clinicians because developing a program to improve patients' engagement with HCP is more feasible than intervening in patients' social capital.

Chapter 2 is the first meta-analysis examining the efficacy of mobile phone reminders on retention to HIV care. Considering that populations affected by the HIV epidemic and modes of HIV transmission differ by countries and regions, the findings from the sub-analyses have important implications for strategic uses of mobile phone technologies to improve retention to HIV care.

Chapter 3 is novel because it is one of the first attempts in the country of Tanzania to examine social capital and social networks in relation to HIV health outcomes. The study also examines factors associated with social capital, an area of limited research available in resource-limited settings. Poverty measured by multidimensional poverty index (MPI) (Oxford Poverty and Human Development Initiative (OPHI), 2015) was a significant predictor of having less social capital among PLWH. In alignment with previous research, social capital is a well-known social determinant of health closely associated with socio-economic status (SES) (Kawachi, Kennedy, & Glass, 1999). However, poverty, as a proxy of SES, was not associated with quality of life in this study, which suggests that the effects of SES may be mediated through social capital.

5.5 Limitations and implications for future studies

This dissertation is based on three independent studies derived from three databases guided by social capital theory. Each chapter clearly reinforces the importance of social capital for the attainment of improved health outcomes among HIV patients. However, given the cross-sectional design of the studies, causal inference should not be drawn from chapter 1 and 3.

It is important to note that the majority of the participants in chapter 1 were males (over 70%) from diverse ethnic backgrounds. Conversely, the majority of the participants in chapter 2 and 3 were women. Therefore, application of the study results should be done carefully.

Both chapter 1 and 3 recruited study participants using convenience sampling. Study participants for chapter 3 were recruited among PLWH who presented to HIV clinics and medical record reviews retrieved past incidences of missed appointment among the participants. Therefore, retention to care was inherently high due to the

sampling method, which limited analysis and inference of retention to care rate as an outcome variable. The followings are recommendations for the future study.

- Outreach and recruit study participants from community who are out of HIV care when using retention to care as a research variable
- Recruit study participants and stratified by HIV prevalence and incidence of study locations and test the effect of gender difference

Both chapter 1 and 3 used self-reported outcome variables. Health related quality of life (QoL) is widely used and well-validated tool however it lacks external validity and does not measure changes over time when it is used in a cross-sectional study.

Therefore use of biomarkers accompanying with self-reported QoL and a longitudinal study design are strongly encouraged. Recommendations for the study are followed.

- Collect biomarkers such as CD4 cell counts, HIV viral loads, weights and WHO HIV stages longitudinally
- Measure changes of self-reported QoL at multiple time points
- Analyze health related QoL by its two factors: physical and mental health

5.6 Suggestions for way forward: social capital and global health

The positive effect of social capital on health is well established and this study elucidates that the effects are consistent among PLWH across regions and populations. People with higher social capital have more access to resources and opportunities, which can be either tangible or intangible, leading to improvement in their health status, wealth, or reputation. However, there is very limited research about how to intervene on social capital. Given limited resources available within a community, this dissertation suggests that the use of mobile technology introduces many opportunities to provide

information, education, resources, and communication at a low cost. Benefits become more visible for people who live in resource-limited settings and in vulnerable situations such as young women of childbearing age. The followings are recommendations for future study using mobile technologies.

- Mobile phone reminders may work differently depending on characteristics of PLWH. Women with babies benefited the most in resource-limited settings, while males living in developed countries did not benefit from the intervention
- Mobile text messages are as effective as mobile phone calls, yet more affordable when designing mobile phone reminder interventions
- Allow bi-directional and personalized mobile text messages instead of automated one-way reminders

This study measured and analyzed social capital at the individual level. One of social capital specific attributes is that it is resource available across different levels. Social capital is not limited to individual social networks but to interpersonal and community level networks. Measuring social capital beyond the individual level will allow for multi-level analysis. This will improve understanding of how to intervene upon social capital in low resource communities burdened with HIV.

References

- Kawachi, I., Kennedy, B. P., & Glass, R. (1999). Social capital and self-rated health: A contextual analysis. *American Journal of Public Health*, 89(8), 1187-1193.
- National Institutes of Health. (2001). *Toward higher levels of analysis: Progress and promise in research on social and cultural dimensions of health.* executive summary. (No. 21-5020).
- Oxford Poverty and Human Development Initiative (OPHI). (2015). Global multidimensional poverty index 2015. Retrieved from http://www.ophi.org.uk/wp-content/uploads/Global-MPI-8-pager_10_15.pdf

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