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Social Isolation and Retention in Care among Older Adults Living with HIV/AIDS

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Doctor of Philosophy

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Social Isolation and Retention in Care among Older Adults Living with HIV/AIDS

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Abstract

Social Isolation and Retention in Care among Older Adults Living with HIV/AIDS
By Moka Yoo-Jeong

Background: Social isolation manifests in objective and subjective forms and affects health care utilization (HCU) behaviors. Yet, studies with persons living with HIV (PLWH) have focused primarily on objective isolation (social network size) and less is known about subjective isolation (loneliness) and its potential influence on HCU behaviors. An essential HCU behavior for positive health outcomes among PLWH is retention in care (RIC), and even less is known among older PLWH. This study sought to identify determinants of loneliness and to explore a path model of social isolation on RIC via emotion dysregulation among older PLWH, guided by the modified Theoretical Model of Loneliness. Differences in characteristics by the levels of RIC were explored.

Methods: Older PLWH (age ≥50) recruited from a single HIV clinic completed a baseline questionnaire on demographics, social network size, loneliness, emotion dysregulation, HIV-related stigma, HIV-disclosure status, depressive symptoms, comorbidities, functional status, and substance abuse. Their RIC (i.e., adherence to HIV medical visits) and clinical data (HIV biomarkers, emergent HCU) were abstracted from electronic medical records (EMR) for 12-months post-baseline. Multivariable linear regression and path analysis were used.

Results: A total of 146 completed the baseline study questionnaire (60% male, 86% Black/African American, M_{age}=56) and 144 had RIC data. Multivariable regression analysis revealed that depressive symptoms and HIV-related stigma explained 41% of the variance in loneliness, controlling for covariates (R^2=0.41, F(7, 138)=13.76, p<0.001). RIC was dichotomized (0=suboptimal [≤85%], 1=optimal appointment adherence [>85%]) and was related to monthly income (B=0.80, p=.07), drug abuse (B=-0.28, p=.02), and baseline CD4+ T cell count (B=1.45, p=.05) in regression analysis. Fit indices reflected a good fit of the proposed path model: χ^2=8.81 (p=.46), CFI=1.00, TLI=1.01, RMSEA<0.001 (90% CI: 0.00-0.09). However, there were no direct or indirect effects of social isolation on RIC.

Conclusions: The current study underscores the importance of targeting HIV-related stigma and depression to reduce loneliness. Socioeconomic and behavioral vulnerabilities including low income and drug abuse are closely linked to suboptimal level of RIC among older PLWH. Focused intervention efforts to reduce disparities in RIC are needed.

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Moka Yoo-Jeong

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CHAPTER 1
INTRODUCTION

Specific Aims

Advancements in antiretroviral therapy (ART) have transformed HIV infection into a chronic condition and have prolonged the longevity of many persons living with HIV (PLWH) in the United States leading to nearly half of the United States HIV population being over 50 years of age by 2017 (Effros et al., 2008). Older PLWH tend to have greater comorbidities than their younger counterparts (CDC, 1998; Grabar, Weiss, & Costagliola, 2006; A. T. Rodriguez-Penney et al., 2013), and have multiple and sometimes conflicting treatment and medication regimens (Holtzman et al., 2013; Tseng, Szadkowski, Walmsley, Salit, & Raboud, 2013), requiring them to have more frequent routine clinic appointments (Buchacz et al., 2008; Gebo et al., 2010). Engagement in routine HIV clinic appointments (i.e., retention in care [RIC]) is crucial for effective treatment and prevention of poor health outcomes, such as development of an AIDS-defining illness, increased odds of mortality, and poorer viral suppression (Giordano et al., 2007; Mugavero et al., 2009; Park et al., 2007; Shapiro et al., 1999; Ulett et al., 2009). However, less than half of all PLWH are retained in care, and only about 30% achieve viral suppression in the United States (Bradley et al., 2014; Gardner, McLees, Steiner, Del Rio, & Burman, 2011).

Social networks and support have long been implicated as important factors for coping with chronic conditions (Gallant, 2003; H. A. van Dam et al., 2005), adherence to medications (DiMatteo, 2004; Magrin et al., 2015), and health care utilization (Broadhead, Gehlbach, deGruy, & Kaplan, 1989; Penning, 1995). Yet, studies indicate that older PLWH are socially isolated and that they report negative mood stemming from loneliness (Grov, Golub, Parsons, Brennan, & Karpiak, 2010; Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005a). Studies examining the effects of social isolation on health outcomes in PLWH have exclusively examined indicators of

objective isolation (i.e., low social network size) and have not assessed both objective and subjective isolation (i.e., loneliness) concurrently, making it difficult to determine why and how social isolation affects health, and what needs to be altered to promote health. Although loneliness is a key correlate of poor health outcomes in the general older adult population (Adam, Hawkley, Kudielka, & Cacioppo, 2006; Caspi, Harrington, Moffitt, Milne, & Poulton, 2006; Cole et al., 2007; L. C. Hawkley, Masi, Berry, & Cacioppo, 2006; L. C. Hawkley, Thisted, Masi, & Cacioppo, 2010; Wilson et al., 2007), and is related to greater use of emergent and unplanned health care service use (Cheng, 1992; Ellaway, Wood, & Macintyre, 1999; Geller, Janson, McGovern, & Valdini, 1999; Genell Andren & Rosenqvist, 1987), only a few studies have examined the effects of loneliness in older PLWH and no studies to date have examined whether RIC is affected when feelings of loneliness or low social network size are present.

Emotion dysregulation is likely to play a key role in the potential association of loneliness and social network size on RIC. Studies in PLWH to date support the link between loneliness and dysregulated emotional states (Grov et al., 2010; Vance, 2006) including depression, which is generally associated with many health-related behaviors like substance/alcohol use, sexual impulsivity, and medication non-adherence (Berking et al., 2011; Gonzalez, Mimiaga, Israel, Bedoya, & Safren, 2013; Pachankis et al., 2015). Similarly, low social networks have been shown to be related to negative mood (Cho, Olmstead, Choi, Carrillo, Seeman, & Irwin, 2018). Dysregulated emotion has also been proposed to predict risky behaviors and/or self-destructive health behaviors (i.e., drug/alcohol use, sexual impulsivity; Berking et al., 2011; Gonzalez et al., 2013; Pachankis et al., 2015). Just as in the previous literature supporting the associations of loneliness, social network size, and negative affective states, we hypothesize that they may also be related to emotion dysregulation. In addition, we hypothesize that emotion

dysregulation will be associated with RIC and that it will mediate the potential association between social isolation and RIC.

Given that this growing population of older adults may require more frequent medical visits and also be at a greater risk for social isolation, understanding whether objective and subjective aspects of social isolation (social network size and loneliness, respectively) affect RIC through mechanisms such as emotion dysregulation, needs to be identified so that interventions to improve RIC among those older PLWH at risk can be developed. Identification of key correlates of loneliness may also help ascertain older PLWH at particular risk for feelings of isolation and its negative health sequelae including potentially poor RIC. The current study proposed to assess factors related to loneliness that may be uniquely present in older PLWH and to assess one potential pathway by which social isolation may affect RIC via emotion dysregulation using modified Theoretical Model of Loneliness as a guiding framework (Hawkley & Cacioppo, 2010).

This study used cross-sectional data to identify factors related to loneliness in 146 older PLWH (50 years old or older). In addition, data on RIC were prospectively collected to evaluate its associations with baseline social isolation (social network size and loneliness) and emotion dysregulation. RIC was assessed via electronic medical records (EMR) over 12-months post-baseline assessment date. The proposed study had the following aims:

Specific Aim 1: To assess the relationship of demographic factors, functional status, HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size to loneliness in older PLWH.

Hypothesis 1. Greater stigma, lower HIV disclosure status, poorer functional status, greater depressive symptoms, and lower social network size will be

associated with greater loneliness.

Specific Aim 2: To assess the relationships of loneliness and social network size with emotion dysregulation and adherence to HIV clinic appointments (i.e., retention in care) in older PLWH.

Hypothesis 2a. Participants with greater loneliness will have greater emotion dysregulation and miss significantly more HIV clinic appointments (direct effects).

Hypothesis 2b. Participants with lower social network size will have greater emotion dysregulation and miss significantly more HIV clinic appointments (direct effects).

Hypothesis 2c. There will be a significant indirect effect of loneliness on adherence to HIV clinic appointments via emotion dysregulation.

Hypothesis 2d. There will be a significant indirect effect of social network size on adherence to HIV clinic appointments via emotion dysregulation.

This study is a first-step towards understanding the impact of social isolation on health, developing targeted interventions to reduce social isolation and manage related outcomes and improving health in this ever-growing population. By identifying factors related to loneliness and examining it as a potential pathway to RIC among older PLWH, the findings from this study may provide ways to identify older PLWH who may be at risk for loneliness, poor RIC, and subsequent negative health outcomes.

Background

Older Persons Living with HIV/AIDS in the United States

According to the Centers for Disease Control and Prevention (CDC), an estimated 45% of persons living with HIV (PLWH) in the United States in 2014 were 50 years old or older (CDC, 2016) and this number is projected to grow to 70% by 2020 (Brooks, Buchacz, Gebo, & Mermin, 2012). There also has been an increase in the HIV incidence among older adults. In 2013, people aged 50 and older accounted for 21% of new HIV diagnoses and 27% of new AIDS diagnoses (CDC, 2015).

Research shows that older PLWH often face increased and complex vulnerability in terms of physical and psychosocial needs. For example, recent works suggest that PLWH may be more vulnerable to early onset of aging, such that they often exhibit more age-associated comorbidities such as cardiovascular diseases or diabetes at a much younger age than their uninfected counterparts (Pathai, Bajillan, Landay, & High, 2014; Guaraldi et al., 2011), indicating that older PLWH may be at a greater physical burden with their natural aging process. Additionally, older PLWH tend to have more chronic and acute morbidities than their younger counterparts (CDC, 1998; Grabar et al., 2006; Rodriguez-Penney et al., 2013), and become involved with multiple and sometimes conflicting treatment and medication regimens (Holtzman et al., 2013; Tseng et al., 2013), requiring them to have more frequent routine clinic visits (Buchacz et al., 2008; Gebo et al., 2010). Health disparities in older PLWH are also reflected in depression, with older PLWH commonly reporting depressive symptoms (Greene et al., 2015; Havlik, Brennan, & Karpiak, 2011) whereas uninfected older adults are less likely to report depression (Fiske, Wetherell, & Gatz, 2009). Studies also indicate that older PLWH tend to live alone and have limited and inadequate social networks compared to their younger counterparts (Schrimshaw & Siegel, 2003;

Shippy & Karpiak, 2005a).

Retention in Care

Regular engagement in HIV medical care, or retention in care (RIC), is a type of treatment adherence behavior in HIV that is critical for health management. RIC is needed to monitor immune function (e.g., CD4+ T cell count), treatment efficacy and toxicities (e.g., HIV-1 RNA levels), and to screen and intervene for other comorbid conditions (Aberg et al., 2009). Studies have shown that failure to be retained in care is significantly related to poorer health outcomes, such as development of an AIDS-defining illness, increased odds of mortality, and poorer viral suppression (Giordano et al., 2007; M. J. Mugavero et al., 2009; Park et al., 2007; Ulett et al., 2009). In addition, the number of missed clinic visits have been found to be a significant predictor of having an AIDS-defining CD4+ T cell count whereas the number of kept clinic visits and regular utilization of HIV medical services predicted non-detectable viral load (van den Berg et al., 2005) and lower utilization of acute and emergent health care services (Shapiro et al., 1999). Therefore, RIC can be conceptualized as a planned and managed behavior that requires effective self-managing skills, which can possibly prevent unplanned, emergent health care utilization behaviors like emergency department (ED) visits or hospitalizations.

Current HIV treatment guidelines in the United States recommend that PLWH should be seen by their healthcare provider every 2-8 weeks when care is initiated and then to be seen at least every 3-6 months once they become immunologically stable and have a suppressed viral load for more than 2 years (Aberg et al., 2014; Deparment of Health and Human Services [DHHS], 2018). However, less than half of all PLWH are retained in care and only about 30% achieve viral suppression in the United States (Bradley et al., 2014; Gardner, McLees, Steiner, Del Rio, & Burman, 20011). Research examining the association between age and RIC has

yielded mixed results with conflicting findings across studies. While some studies report that younger age is associated with lower RIC (Fleishman, Yehia, Moore, Korthuis, & Gebo, 2012), differences between young and old groups are often small and some are contradictory (Bodenlos et al., 2007). Moreover, a recent study using CDC surveillance data from 2009 found that among newly diagnosed patients, RIC is lower among older PLWH than their younger counterparts (Hall et al., 2012). It is *unknown* whether there is a subgroup of patients *within* the older HIV group that may be poorly retained in care and thus have increased risk for morbidity and mortality.

There is no "gold standard" for assessing RIC care and it can be operationalized with multiple indicators using any combination of kept clinic visits and 'no show' or missed clinic visits over a specified time interval (e.g., 6-month care gaps with no visits, visits in 3-month over 12 month time frame) based on the study or clinic context (Mugavero, Davila, Nevin, & Giordano, 2010; Mugavero et al., 2012). For the purpose of this study, kept, missed, and canceled visits with HIV primary medical providers were systematically captured from the available electronic medical records (EMR) and RIC was operationalized by *appointment adherence*. Detailed information on appointment adherence is found in the methods section (p.20).

Social Isolation

Social networks and social support have long been recognized as important factors for coping with chronic conditions (Gallant, 2003; van Dam et al., 2005), adherence to medications (DiMatteo, 2004; Magrin et al., 2015), and health care utilization (Broadhead et al., 1989; Penning, 1995) in both HIV-infected and uninfected individuals. Studies show a consistent association between social support and adherence, suggesting that health may be a downstream

factor affected by the effects of social support on adherence. Two meta-analyses showed that functional support (i.e., emotional/perceived support, informative/instrumental support), rather than structural support (i.e., marital status, living arrangement, network size) was more strongly associated with treatment adherence (DiMatteo, 2004; Magrin et al., 2015). On the other hand, a study by Bodenlos and colleagues found that structural support (i.e., social network size), rather than functional support (i.e., perceived satisfaction with support), was related to appointment adherence in a sample of PLWH (Bodenlos et al., 2007). Similarly, Waldrop-Valverde and colleagues found that available support moderated the effect of neurocognitive impairment on appointment adherence among PLWH; those with impaired neurocognitive function and higher use of support were less likely to miss HIV clinic appointments (Waldrop-Valverde, Guo, Ownby, Rodriguez, & Jones, 2014). This study also showed main effects of social support on higher appointment adherence demonstrating the importance of examining whether older PLWH possess adequate social network size and support systems. However, recent studies suggest that those aging with HIV are socially isolated; they tend to live alone and have limited and inadequate social networks compared to their younger counterparts (Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005a), and report negative mood stemming from loneliness (Grov et al., 2010). HIV infection has long been associated with stigma that often affects those who are socially disenfranchised, which may render PLWH to be chronically marginalized and isolated. HIV-related stigma may also alter the dynamics of the infected person's social structures and relationships and may affect participation in social activities or roles. However, social isolation has been addressed only to a limited degree in the context of aging/older individuals with HIV and it remains unknown whether and how social isolation affects RIC.

Definition of Social Isolation

The definition of social isolation has often been varied in the literature; while some studies conceptualize and define social isolation with a unidimensional approach focusing on quantifiable constructs such as the lack of social integration or social contacts, some studies argue that social isolation has multidimensional aspects that incorporate both objective and subjective constructs (Dickens, Richards, Greaves, & Campbell, 2011). A recent concept analysis paper on social isolation supports the latter notion and notes that social isolation is "a state in which the individual lacks a sense of belonging socially, lacks engagement with others, has a minimal number of social contacts and they are deficient in fulfilling and quality relationships" (Nicholson, 2009, p.1346). Similar to this multidimensional concept of social isolation, Cornwell and Waite defined social isolation by incorporating two distinct but related concepts—*social disconnectedness* and *perceived isolation*— in their study of a nationally representative population of community-residing older adults (Cornwell & Waite, 2009a; Cornwell & Waite, 2009b). These researchers note that the use of the multidimensional definition of social isolation in research allows for clearer understanding of how and what aspect of isolation truly affects a person's health (Nicholson, 2009; Cornwell & Waite, 2009b).

Social disconnectedness is the objective aspect of social isolation and is indicated by contextual factors including small social network size or low levels of participation in social activities (Cornwell Waite, 2009a; Cornwell & Waite, 2009b). Social disconnectedness affects an individual's access to material resources such as information, transportation, financial loans, or tangible support (Haines & Hurlbert, 1992; van Olphen et al., 2003). Studies with general older adults with or without comorbid conditions show that indicators of social disconnectedness, such as small social network size, predict morbidity and mortality and recent hospitalization or ED

visits (Aminzadeh & Dalziel, 2002; Brummett et al., 2001; Rodriguez-Artalejo et al., 2006).

Perceived isolation is the subjective aspect of social isolation that results from unfulfilled intimate and social needs for support (e.g., low quality, emotionally distant, unsatisfying) and is indicated by feelings of loneliness or perceived lack of support (Cacioppo, Hawkley, & Thisted, 2010; Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006; Peplau & Perlman, 1982; Peplau, M. & Morasch, B., 1982). The key term in this definition is perception, meaning that individuals can live solitary lives or be objectively isolated and not feel lonely. Alternately, they might be socially connected with a large number of social network members and yet experience feelings of loneliness. Loneliness is potentially modifiable (Masi, Chen, Hawkley, & Cacioppo, 2010), and is directly associated with various health outcomes including elevated blood pressure in both cross-sectional and longitudinal studies (Hawkley et al., 2006; Hawkley et al., 2010), increased risk for cognitive decline or Alzheimer's disease (Wilson et al., 2007), changes in gene expression for inflammation (Cole et al., 2007), and negative affective states (Cacioppo et al., 2006; Weeks, Michela, Peplau, & Bragg, 1980).

While both aspects of social isolation are linked to numerous health outcomes in the general middle-age to older-aged adults, findings related to the subjective dimension of isolation are scant in the HIV and aging literature compared to the studies of the objective dimension of isolation. Because both components of social isolation may affect health in different ways (Cornwell & Waite, 2009b; Holt-Lunstad, Robles, & Sbarra, 2017), exploration of determinants and consequences of either component is fundamental to understand the association between social isolation and health outcomes. In this study, we focused on *social network size* and *loneliness* as indicators for objective and subjective aspects of social isolation, respectively, with the emphasis on exploring correlates of loneliness in our sample of older PLWH and assessing

the effects of both indicators on RIC.

Loneliness

Studies in general mid-age to older adults indicate that up to 40% perceive themselves as lonely (Golden et al., 2009; Routasalo, Savikko, Tilvis, Strandberg, & Pitkala, 2006; Savikko, Routasalo, Tilvis, Strandberg, & Pitkala, 2005). Although the prevalence estimate of loneliness in older PLWH is unknown, it may be particularly severe for them, especially as they experience reduced social network size for various reasons including age-related changes (reduced functionality, deaths of peers, empty nest), HIV-related stigma and discrimination, and self-protective withdrawal from society (Emlet, 2006b; Rabkin, McElhiney, & Ferrando, 2004; Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005a; Shippy & Karpiak, 2005b). Aging with HIV has been reported as more stigmatizing because older age is associated with negative stereotypes like incompetence and frailty, and HIV infection has long been associated with judgment and social exclusion (Emlet, 2006a). Stigma can be internalized and can lead to feelings of shame, difficulty reaching out to others, and "silencing" HIV status because of fear of rejection, which may increase a sense of loneliness, promote self-protective withdrawal, and limit much needed support from others (Beuthin, Bruce, & Sheilds, 2014; Emlet, 2006b; Emlet,2007). This internalized stigma and feelings of loneliness may induce symptoms of depression or they may instead be the consequences of depression. Moreover, Grov et al. (2010) found that HIV-related stigma and loneliness explained a significant variability in depressive symptoms in their sample of older PLWH.

Identification of unique correlates of loneliness is critical to developing targeted interventions to reduce loneliness in older PLWH and understanding its possible downstream

effects on health, but they have not yet been investigated. One study suggests that stigma and HIV-disclosure status may affect loneliness. A qualitative study of 52 HIV-infected drug users found that social marginalization as a result of HIV-related stigma led individuals to perceive themselves as isolated and that disclosure of HIV status was a common barrier to social relationships (Ware, Wyatt, & Tugenberg, 2006). The participants reported that loneliness stimulated their desire to connect with others, which often led to risky behaviors (e.g., drug use; Ware et al., 2006). In a study examining chronic sorrow in PLWH, women with children, particularly African American (AA) women, were more stigmatized and isolated than gay men, which conferred feelings of loneliness (Lichtenstein, Laska, & Clair, 2002). Studies with uninfected older adults suggest a number of predictors of loneliness. Hawkley et al. (2008) used a conceptual framework of social networks (Berkman, Glass, Brissette, & Seeman, 2000) to examine factors related to loneliness in a sample of 225 uninfected middle-aged and older adults living in the United States and found that demographic factors (age, gender, race/ethnicity), functional status, and social network size explained about 37% of the variance in loneliness (Hawkley et al., 2008), which was similar to other studies (Cohen-Mansfield & Parpura-Gill, 2007; Theeke, 2009). The current study assessed HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size to loneliness while controlling for significant demographic factors, functional status, and comorbidity burden.

Social Isolation and Health Care Utilization Behaviors

In the HIV literature, the focus of social isolation has primarily been on the objective component of social isolation (i.e., social network size) and no studies have investigated the two components of social isolation simultaneously, making it difficult to determine why and how

social isolation affects health. For example, a study on aging veterans found that social isolation was associated with greater risk of hospitalizations and death for both HIV-infected and uninfected veterans. Although statistically non-significant, seropositive veterans were more socially isolated, particularly in the oldest individuals (Greysen et al., 2013). However, the study operationalized social isolation only through the objective indicators (i.e., social network size such as number of frequent contact and marital status) and did not consider loneliness. The results point to a number of unanswered questions. How and why does social network size affect hospitalization? Does loneliness that could stem from low social network size somehow affect RIC, a managed behavior that could potentially prevent acute hospitalization? It is widely known that social isolation is harmful to health, yet the underlying mechanisms to explain why are not well understood especially in this growing subpopulation of PLWH.

The extent to which social network size and loneliness affect RIC among older PLWH is unknown. Existing studies on the effects of loneliness on health care utilization (HCU) behaviors among uninfected individuals primarily focus on unplanned, emergent HCU rather than planned health care visits. In a cross-sectional study of 164 ED users, loneliness was associated with total number of ED visits over the previous year, with greater loneliness predicting greater ED visits (Geller et al., 1999; Genell Andren & Rosenqvist, 1987). Although these studies show that loneliness is associated with emergent HCU, they are limited by the use of cross-sectional designs to identify predictors of HCU behaviors and self-report of health care service use. Studies also show that greater loneliness is associated with greater frequency of primary care clinic visits with healthcare providers (Cheng, 1992; Ellaway et al., 1999). However, it is not clear whether the visits with healthcare providers operationalized in these studies were planned, scheduled visits or unplanned, emergent visits. Blurred distinctions between planned versus

unplanned/urgent attendance at primary clinics makes it difficult to interpret this set of findings in relation to RIC in older PLWH, where RIC is conceptualized as more intentional self-management behavior, whereas urgent and unplanned clinic visits are not conceptualized in this way. To our knowledge, only one study has examined the effects of loneliness on planned HCU behavior. In a cross-sectional study of a nationally representative sample of 2,033 uninfected older adults (≥65 years of age) in Ireland, loneliness was associated with ED visits but not with *planned* hospital admissions, independent of social participation, social support, and depression (Molloy, McGee, O'Neill, & Conroy, 2010). However, this study is limited by its retrospective self-report over the previous year's healthcare service use and the use of a single-item to assess for loneliness. Drawing from the studies showing higher use of ED in relation to higher levels of loneliness in uninfected adults and previous studies showing the effect of structural social support on adherence to medical appointments in PLWH (Bodenlos et al., 2007; Waldrop-Valverde et al., 2014), our study postulated that older PLWH with greater loneliness and small social network size may be less likely to be retained in care.

Emotion Dysregulation

Emotion regulation is the process by which individuals manage both positive and negative emotions (Gross, 1998) and may be a particularly important regulatory domain in controlling and managing behaviors (Tice & Bratslavsky, 2000). Emotion dysregulation, defined as difficulties in self-regulation of thoughts and emotions and control over affect-driven behaviors (Mennin, Heimberg, Turk, & Fresco, 2005), might operate as a key mechanism in explaining the effect of social isolation on RIC in older PLWH for three reasons below.

First and foremost, emotions are recognized as both processes and byproducts of social

interactions (Cole, Martin, & Dennis, 2004). Emotions can be shaped and altered by traumatic events that may influence social relationships. HIV has been associated with multiple layers of stigmas and individuals living with HIV may have been exposed to social rejections or perception of such rejections. Difficulties in emotion regulation arise from early exposure to stressful interpersonally rejecting and isolating environments (Shields, Cicchetti, & Ryan, 1994), thus emotion dysregulation may be prevalent in PLWH. These exposures and experiences may limit social network size and promote feelings of loneliness for many older individuals aging with HIV.

Second, loneliness may pose an additional threat to emotion regulation; when the need for companionship is consistently unfulfilled in individuals' perception, they may become distressed and experience negative affective states like depression. Emotion dysregulation has been shown to be associated with negative affective states, including anxiety and depression, in studies with PLWH (Brandt, Zvolensky, & Bonn-Miller, 2013). Evidence shows that lonely individuals exhibit higher levels of negative affect and lower levels of positive affect than individuals who are not lonely (Louise C Hawkley, Preacher, & Cacioppo, 2007) and similar association, especially on depression, is shown with small social network size (Cho, Olmstead, Choi, Carrillo, Seeman, & Irwin, 2018). Similarly, studies with older PLWH have shown that loneliness is associated with depression (Grov et al., 2010; Vance, 2006), yet there is no study linking the relations of loneliness, social network size, and emotion dysregulation in older PLWH.

Third, in addition to conferring risk for negative affective symptoms, dysregulated emotion has also been proposed to predict risky behaviors and/or self-destructive health behaviors (i.e., drug/alcohol use, sexual impulsivity; Berking et al., 2011; Gonzalez et al., 2013;

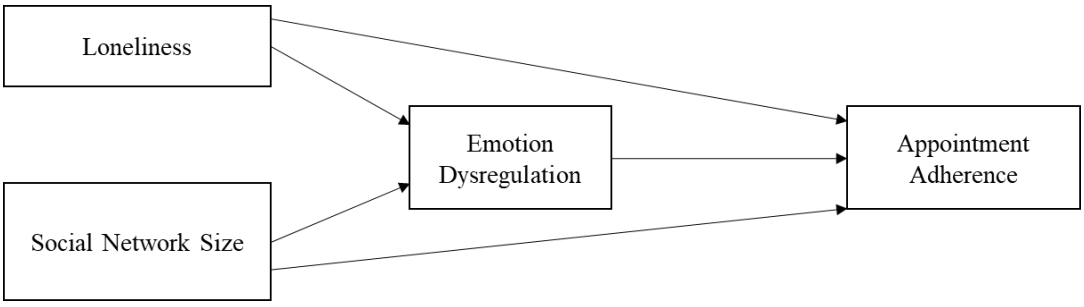
Pachankis et al., 2015). In light of health behaviors, a recent study showed a moderating effect of emotion dysregulation in the association between depression and HIV medication adherence (Brandt, Bakhshaie, Zvolensky, Grover, & Gonzalez, 2015). However, no research has examined emotion dysregulation in relation to RIC in older PLWH. Just as depression is associated with medication adherence, we hypothesize that emotion dysregulation may be associated with RIC in older PLWH. Although the effect of social isolation on emotion dysregulation has not been examined to date, to the extent that both indicators of social isolation are associated with negative affective states, it is postulated that social isolation would be associated with emotion dysregulation. In turn, emotion dysregulation might contribute to a reduced motivation to engage in health behaviors, such as RIC. The current study tested the hypothesis that emotion dysregulation may be associated with social isolation and that emotion dysregulation mediates the association between social isolation and RIC.

Conceptual Framework

Hawkley and Cacioppo (2010) suggest in their Theory of Loneliness that lonely people feel unsafe in their social environment and these feelings perpetuate them to become overly vigilant for social threats, thereby diminishing their capacity to self-regulate emotions and behaviors (Cacioppo & Hawkley, 2009; Hawkley & Cacioppo, 2010). In other words, when the feelings of loneliness become chronic and persistent sources of distress, the ability to regulate emotion becomes reduced, leading to dysfunctional health behaviors, and subsequently affecting health outcomes. The theory also assumes that the harmful effects of loneliness may develop over time and that as people age, loneliness can escalate the risk factors of detrimental health outcomes much more quickly (Hawkley & Cacioppo, 2010). In our study, social network size

was added as an exogenous variable to test the two aspects of social isolation simultaneously on RIC either directly or indirectly via emotion dysregulation (**Figure 1.1**). We hypothesize that both social network size and loneliness will have a direct effect on RIC and also an indirect effect through emotion dysregulation among our sample of older PLWH. We also explored the differences in participant characteristics depending on their level of RIC.

Figure 1.1 Hypothesized *a priori* Model of Social Isolation and Retention in Care



Methods

Research Design: This study employed a cross-sectional, descriptive design to identify factors related to loneliness in 146 older PLWH (≥ 50 years old). The study also incorporated a prospective data collection of RIC. A sample of HIV-infected older adults enrolled at a large comprehensive metropolitan HIV care clinic located in the southeast region of the United States, was recruited through flyers, word of mouth, and healthcare provider referrals from August 2016 to April 2017.

Inclusion Criteria include English-speaking individuals, age 50 years old or older, diagnosed with HIV/AIDS, and having at least one medical visit established in the recruiting clinic.

Exclusion criteria: severe learning disabilities, intellectual disabilities, psychotic disorders, and severe cognitive impairment/dementia that inhibits an individual's ability to consent to the study

and complete study assessments. These exclusion criteria were screened and confirmed by review of the EMR. A consent post-test designed to document capacity to provide informed consent was given to assess the capacity to provide informed consent prior to enrollment. Those who failed to pass the test within three attempts were excluded (n=3).

Rationale for Sample Characteristics: HIV infected individuals who are 50 years old or older are selected. While 50 years of age is not generally used to identify "elderly" patients, this age cut-off is frequently used by the Center for Disease Control (CDC) and other AIDS agencies when reporting statistics related to older PLWH.

Setting & Human Subjects Involvement: Emory University Nell Hodgson Woodruff School of Nursing served as the coordinating center for this study. Participants were recruited from a large HIV outpatient clinic in the Southeast region of the United States. In 2013, this clinic served a total of 5,416 HIV+ patients, 2,559 between the ages of 45-64, and 131 of them older than 65 years.

Recruiting Clinic Characteristics: The recruiting clinic is a Ryan White funded clinic that adheres to the US treatment guidelines recommendations and also has specific and stringent regulations for clinic patients where if the patients miss their clinic appointments with their HIV care provider for more than 6 months, they are required to go through the arduous process of re-enrollment in the clinic. Additionally, if the patient is receiving AIDS Drug Assistance Program (ADAP), he or she must adhere to routine lab appointments every 6 months and also pick up ART from the pharmacy regularly to stay enrolled in the ADAP program. The clinic is an integrated clinic where it provides interdisciplinary care to HIV-infected patients. It provides not only the primary HIV care, but also dental, pharmacy, women's health, and psychiatric services to the patients all within the clinic. There is an acute care services dedicated in the clinic where if

a scheduled or walk-in patient present in the clinic has an acute issue, this patient is sent to the special area ("treatment and holding") and receives immediate treatment there (e.g., IV fluids, blood, lumbar puncture, respiratory therapy) or admitted directly to the affiliated hospital nearby.

Data Collection and Procedures: Following an initial start-up period for IRB approval, ordering supplies, and obtaining a partial HIPAA waiver from Emory University's IRB to allow the PI to screen patient medical charts for potential eligibility, active recruitment for the study began. All study protocols and informed consent were reviewed and approved by Emory University Institutional Review Board and recruiting clinic's and its affiliated hospital's Research Oversight Committee. Flyers describing general study information were posted in the recruiting clinic with contact information of the PI. The PI discussed the study with individuals who were interested and established study eligibility for those with continued interest. Written informed consent were obtained prior to data collection. Participants were informed of the potential risks and benefits, and they had the right to withdraw their participation in the study at any time without prejudice. Participants were asked to consent to provide access to their medical records in order to assess RIC over 12-month post-baseline assessment date. After obtainment of informed consent, participants completed the baseline study questionnaires in one session held in a private office at either the recruiting clinic or the school of nursing. Data were collected via Research Electronic Data Capture (REDCap) on a computer. REDCap is a secure, web-based, electronic data capture tool allowing online survey entry (Harris et al., 2009) in compliance with the University's HIPAA policies and procedures. All individuals were first taught on how to use the computer and sample questions were provided for practice. Total time to complete the questionnaires was approximately 45-60 minutes. Potential risks of the study were minimal but included the possibility of distress and fatigue during or after the questionnaire administration. In order to

reduce distress and fatigue, participants were given time to rest or to use the restroom anytime during the study assessments. Participants were compensated $25 in cash upon completion for their participation. All analyses and study procedures complied with HIPAA regulations and federal regulations for the protection of human research subjects and inclusion of women and minorities.

Recruitment started in August 2016, with 146 subjects recruited in April 2017, and prospective EMR data abstraction for RIC started in August 2017 and ended in April 2018. Over the 12-month data collection period, information on the dates and the status of HIV medical visits were abstracted from patient medical records from August 2017 to April 2018. Consistent with other studies and definitions, HIV medical visits were defined as visits made to a HIV medical provider including the MD, DO, PA, and NP in the ambulatory setting. Specialty care visits (e.g., mental health, cardiology, etc.), annual well-visits including gynecologic visits, walk-in visits, nurse visits (e.g., B12 injection, wound management, etc.), and phlebotomy visits were excluded. HIV medical visit status were coded as attended, no-show, or canceled. A visit was considered missed if the status was “no-show” and not missed if the status was “attended.” A visit that was cancelled either by the provider or the patient was excluded from the calculation of RIC (i.e., appointment adherence). Approximately 10% of all data were randomly re-abstracted by the PI again to ensure the quality of the data and to minimize discrepancies and errors. Of the total 146 participants enrolled in the study, two participants had no information on RIC (i.e., no visits scheduled since the baseline visit), thus was removed from the analysis for aim 2.

Data Management: All participant records including the consent forms are stored in a locked file cabinet in the research office and accessible only to the PI. All data maintained in the computerized database are accessible only with a login and protected, encrypted password. All

data are coded by subject identification number and no identifying information are recorded on the data collection forms. The master list that will connect the codes to identifying information are secured in the research project office. EMR abstraction was done only by the PI in a private office.

Potential Benefits of the Research to the Subjects: There were no direct benefits to the participants beyond the opportunity to improve the health of future older PLWH. Younger PLWH and HIV care providers may benefit from the research through a greater understanding of social isolation and potentially modifiable factors for loneliness and factors related to retention in care.

Importance of Knowledge to be Gained: Understanding unique psychosocial challenges faced by older PLWH and how it affects health outcomes and self-management behavior, particularly retention in care, are critically important and are the priorities of NIH Office of AIDS Research and US National HIV/AIDS Strategy (White House Office of National AIDS Policy, 2015). As many individuals with HIV/AIDS are aging in the United States and all around the globe, information gained from this study will be vital to designing and implementing future interventions to reduce loneliness and improve its related health outcomes among older PLWH.

Measures

A demographic questionnaire was utilized to collect demographic information on age, race/ethnicity, gender, sexual orientation, level of education, monthly household income, time since HIV diagnosis, history of homelessness in the past 12 months, health insurance coverage, substance use, transportation, and satisfaction with clinic (i.e., patient-provider relations). HIV status as indicated by CD4+ T cell count and HIV-1 viral load were collected from EMR.

Depressive symptoms was assessed using the Center for Epidemiologic Studies Depression Scale Revised (CESD-R). The original scale was created by Radloff (1977), and was

revised by Eaton, Smith, Ybarra, Muntaner, and Tien (2004). The CESD-R contains 20 items that assess nine symptoms of depression (dysphoria, anhedonia, appetite, sleep, concentration, worthlessness, fatigue, agitation, and suicidal ideation) in accordance to the Diagnostic and Statistical Manual (DSM-V) diagnostic criteria for Major Depressive Disorder. Participants answer 0="Not at all or less than one day" to 3="Nearly every day for 2 weeks," with possible scores ranging from 0 to 60. A score ≥ 16 indicates at risk for clinical depression. The scale has good validity and internal consistency (N. T. Van Dam & Earleywine, 2011) and the Cronbach's α was 0.93 in our sample.

Functional status was measured using a modified version of Lawton and Brody's Instrumental Activities of Daily Living Scale (IADL),(Lawton & Brody, 1969) which consists of self-reported levels of functionality on numerous daily tasks (e.g., managing finances, medication adherence, employment, etc.). It is also used as an indicator of the severity of chronic illness and to evaluate whether the skills needed to live independently are present in an individual. The IADL has been used frequently in HIV research.

Comorbidity burden was measured using self-reported version of the Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987). The CCI includes 19 conditions in which participants were asked to rate "Yes" on the conditions that they were diagnosed with. These conditions include myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, gastrointestinal disease, and mild and serious liver disease, uncomplicated and complicated diabetes mellitus, hemiplegia, moderate and severe renal disease, cancer, leukemia, lymphoma, and secondary metastasis. The comorbidities were assigned with a weight based on the adjusted 1-year mortality risk (Charlson et al., 1987). AIDS

diagnosis was omitted from the CCI in our study as its weight is outdated in the current era of cART (Zavascki & Fuchs, 2007) and age was not adjusted. The CCI has strong construct validity and reliability (S. F. Hall, 2006) and has been used in previous studies with PLWH (Lohse et al., 2011; Rodriguez-Penney et al., 2013).

HIV-related stigma was measured with Kalichman et al.'s Internalized AIDS-Related Stigma Scale (Kalichman et al., 2009), which is a self-report of 6 items rated dichotomously (1=agree, 0=disagree). Questions include: "It is difficult to tell people about my HIV infection"; "being HIV positive makes me feel dirty"; "I feel guilty that I am HIV positive"; "I am ashamed that I am HIV positive"; "I sometimes feel worthless because I am HIV positive"; and "I hide my HIV status from others". A higher score is indicative of greater stigma. This scale was developed with nearly 3,000 HIV positive persons in South Africa, Swaziland, and Atlanta, GA and shows good internal reliability (α= .73 to .76) and criterion validity. The Cronbach's alpha for our sample was 0.83.

HIV-disclosure status was assessed by asking the participants whether they disclosed their HIV status to someone. Participants were dichotomized into two groups based on their response (0=disclosure to no one, 1=disclosure to someone).

Social network size was measured using Social Network Index (SNI), which assesses participation in 12 types of social relationships or social activities at least once every 2 weeks in person or on the phone (Bickart, Wright, Dautoff, Dickerson, & Barrett, 2011; Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). The types of social relationships or activities include relationships with a spouse, parents, parents-in-law, children, other close family members, close neighbors, friends, colleagues/coworkers, schoolmates, fellow volunteers, members of groups without religious affiliation, and members of religious groups (Cohen et al., 1997). The total

number of people with whom the participants have regular contact was summed across the 12 possible social relationships, reflecting the *overall network size*. A higher score indicates more social connectedness. SNI was utilized on a sample of older adults in a number of studies (Bickart et al., 2011; Cohen et al., 1997).

Loneliness was measured using the Short Form 8a of the Patient-Reported Outcomes Measurement Information System (PROMIS)-Social Isolation (SI) item bank. The PROMIS measures are standardized based on common metrics that allow for comparisons across domains, across chronic diseases, and with the general population (Cella et al., 2007). PROMIS-SI instrument uses 8-items to assess *perceptions* of being avoided, excluded, detached, disconnected from, or unknown by others on a 5-point Likert scale (1=Never to 5= Always; PROMIS, 2015). Items were scored using the total raw score by summing the values of the response to each question, with possible scores ranging from 8 to 40. A higher score indicates greater loneliness.

Emotion dysregulation was measured using Gratz and Roemer's Difficulties in Emotion Regulation Scale (DERS) (Gratz & Roemer, 2004), which was developed to assess multiple aspects of emotion dysregulation and includes 36-items rated on a 5-point Likert scale (1=Almost never to 5=Almost always). DERS contains 6 subscales that are important for emotion regulation: non-acceptance of emotional responses, difficulties engaging in goal-directed behaviors, impulse control difficulties, lack of emotional awareness, limited access to emotion regulation strategies, and lack of emotional clarity. Higher scores suggest greater problems with emotion regulation. DERS has high internal consistency (Cronbach's α from .80 to .89), internal consistency test–retest reliability (r = .88), and adequate construct and predictive validity among adolescents, young adults, and community dwelling older adults (Staples & Mohlman, 2012). For the current study, the global emotion dysregulation composite score was

utilized.

Retention in care was operationalized by *appointment adherence*, which was computed by calculating the number of attended HIV medical visits in the numerator and the number of total scheduled visits (attended plus missed visits) in the denominator during the 12-month prospective observation period (Mugavero et al., 2010). A visit that was cancelled either by the provider or the patient was excluded from the calculation.

Sample size: Power Analysis and Sample Size (PASS) software was used for sample size calculation for aim 1. The effect size was determined based on previous studies examining predictors and outcomes of loneliness in the general older adult population and older PLWH (Grov et al., 2010; Mackin & Arean, 2007; Theeke, 2009). It was calculated that a sample size of 140 achieves 85% power to detect a difference in correlation of 0.25 at 5% significance level, and achieves 87% power to detect an R^2 of 0.08 attributed to 2 independent variable(s) using an F-Test at alpha=0.05. The variables tested will also be adjusted for additional independent variables with an R^2 of 0.03.

For aim 2, classical path analysis was used to test the simultaneous effects of loneliness and social network size on retention in care (*appointment adherence*, defined by the percentage of attended HIV medical visits out of the total scheduled visits). The sample size calculation for the path analysis used the method of MacCallum and Hong (MacCallum & Hong, 1997), based on Goodness of Fit Index (GFI). It was calculated that with an alpha=0.05, and the given number of parameters (6) and variables (4) in the proposed model, we could detect a difference of 0.10 (GFI=0.9 vs GFI=0.8) with an n=119. Thus the current sample size of 146 was adequate for testing effects in the proposed path model.

Data Analysis

Descriptive statistics was analyzed for all study variables with examination of type and extent of missing data. Any missing data were checked for bias (predictors of missing) using sensitivity analysis and assessed for assumptions of missing completely at random/missing at random. Appropriate correlational analysis, ANOVA, and Chi-square tests were performed for each of the independent variables as well as with the outcome variables in order to identify factors which are likely to be either indicators of outcome variables for two aims or are likely to confound the relationship between the variables of interest and outcome variables. Factors that were considered as potential confounders are those observed to have moderate associations with outcome variables as well as with independent variables specified in the hypotheses. These variables were controlled in the analyses for specific hypotheses as appropriate. Data were checked for distributional assumptions and independence of observations using histograms and residual plots and appropriate data transformations will be made as necessary. Outliers and influential data points were analyzed as well as multicollinearity using tolerance and variance inflation factors and condition index. Data analyses employed SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.) and MPlus statistical software version 8.2 (Muthén and Muthén. Released 2018. MPlus for Windows, version 8.2. Los Angeles, CA: Muthén and Muthén). Significance for all hypotheses tested were set at an alpha of 0.05, unless specified otherwise.

Specific Aim 1: To assess the relationship of demographic factors, functional status, HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size to loneliness in older persons living with HIV/AIDS.

Hypothesis 1. Greater stigma, lower HIV disclosure status, poorer functional status, greater depressive symptoms, and lower social network size will be associated with greater loneliness.

Bivariate relationships between independent variables and loneliness were determined using Pearson's correlation. Hierarchical linear regression analysis was used to statistically evaluate the association between loneliness and independent variables, adjusting for covariates found significant from the bivariate analyses.

Specific Aim 2: To assess the relationships of loneliness and social network size with emotion dysregulation and adherence to HIV clinic appointments in older persons (i.e., retention in care) living with HIV/AIDS.

Hypothesis 2a. Participants with greater loneliness will have greater emotion dysregulation and miss significantly more HIV clinic appointments (direct effects).

Hypothesis 2b. Participants with lower social network size will have greater emotion dysregulation and miss significantly more HIV clinic appointments (direct effects).

Hypothesis 2c. There will be a significant indirect effect of loneliness on adherence to HIV clinic appointments via emotion dysregulation.

Hypothesis 2d. There will be a significant indirect effect of social network size on adherence to HIV clinic appointments via emotion dysregulation.

All hypotheses were tested within a single path analysis. The focus was on the significance (or lack of) the tests of direct and indirect effects. Overall goodness of fit indices (CFI, TLI, and RMSEA) was also checked to see if any modifications to the proposed model lead to a more accurate model, and we interpreted the model with the best fit.

Outline of the Dissertation

Three manuscripts written for publication in a peer-reviewed journal are included in this dissertation, including a detailed, literature synthesis of loneliness in older PLWH (**Chapter 2**), and two manuscripts addressing the specific aims of this study (**Chapters 3** and **4**). A comprehensive summary of the results of this study, as well as implications for future research, practice, and policy are included in **Chapter 5**.

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CHAPTER 2

A SYSTEMATIC REVIEW OF LONELINESS IN OLDER PERSONS LIVING WITH HIV/AIDS

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Abstract

Although loneliness has been linked to numerous health outcomes in older adult populations, there is limited understanding about loneliness among older persons living with HIV (PLWH). The purpose of this systematic review was to explore the current state of science regarding loneliness and to identify correlates of loneliness in older PLWH. A comprehensive literature search guided by the PRISMA statement was conducted using electronic databases, such as PubMed, PsycINFO, Embase, and CINAHL. Seven studies met inclusion criteria. All studies employed cross-sectional and descriptive designs, and mostly used secondary datasets (n=5). Sample sizes ranged from 96 to 914. All studies assessed loneliness with either the De Jong Geirveld Loneliness Scale or the University of California Los Angeles Loneliness Scale, in various versions. The majority of studies included in the review reported some levels of loneliness among the samples. Sociodemographic factors (age, race/ethnicity, sexual orientation, gender), HIV-related stigma, risky behaviors (unprotected sex, substance use), and clinical outcomes (depression, quality of life, functional status, cognitive function) were related to loneliness. Nurses working closely with older PLWH are in key positions to assess for loneliness and offering available resources. Additional research is needed to deepen our knowledge of loneliness and its association with health in this ever-growing population of older adults.

Key words: loneliness, social isolation, older adults, stigma, HIV, systematic review

A Systematic Review of Loneliness in Older Persons Living with HIV/AIDS

Introduction

Advances in antiretroviral therapy (ART) have transformed HIV infection into a chronic condition and prolonged the life expectancy of persons living with HIV (PLWH). According to the Centers for Disease Control and Prevention (CDC), an estimated 45% of PLWH in the United States in 2014 were 50 years old or older (Centers for Disease Control and Prevention [CDC], 2016) and this number is projected to grow to 70% by 2020 (Brooks, Buchacz, Gebo, & Mermin, 2012). Older age is a state of vulnerability in terms of social context where physical disability, life course transitions, and the death of family members or friends may all contribute to restricted social contacts and risk for social isolation (Victor & Bowling, 2012). Older PLWH may be particularly susceptible to social isolation due to living with a highly stigmatized disease, and the risk for non-disclosure of HIV status that may limit access to appropriate support when needed. In fact, studies suggest that older PLWH tend to live alone and have limited and inadequate social networks compared to their younger counterparts (Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005) and report negative mood stemming from loneliness (Grov, Golub, Parsons, Brennan, & Karpiak, 2010). HIV infection has long been associated with stigma that often affects those who are socially disenfranchised, which may render PLWH to be chronically marginalized and isolated. HIV-related stigma may also alter the dynamics of the person's social structures and relationships and may affect participation in social activities or roles and feelings of perceived isolation and support. However, social isolation has been addressed only to a limited degree in the context of aging/older PLWH.

Social isolation is defined as "a state in which the individual lacks a sense of belonging socially, lacks engagement with others, has a minimal number of social contacts and they are

deficient in fulfilling and quality relationships" (Nicholson, 2009, p.1346), and can be assessed objectively by the number of social network size and subjectively by feelings of isolation or loneliness. While both aspects of social isolation are prevalent and linked to numerous health outcomes for adult populations, findings related to the subjective dimension of isolation are scant in the HIV and aging literature compared to the studies of the objective dimension of isolation. Because both components of social isolation may affect health in different ways (Cornwell & Waite, 2009; Holt-Lunstad, Robles, & Sbarra, 2017), exploration of determinants and consequences of either component is fundamental to understand the association between social isolation and health outcomes. Therefore, the focus of this review was on the subjective aspect of social isolation—or *loneliness*—rather than the objective social isolation.

Persistent feelings of loneliness are increasingly recognized as a significant public health concern and have been linked to numerous adverse outcomes in the studies among uninfected adults, including increased mortality (Holt-Lunstad, Smith, Baker, Harris, & Stephenson, 2015), increased coronary heart disease (Valtorta, Kanaan, Gilbody, Ronzi, & Hanratty, 2016), elevated blood pressure (Hawkley, Masi, Berry, & Cacioppo, 2006; Hawkley, Thisted, Masi, & Cacioppo, 2010), increased risk for cognitive decline or Alzheimer's disease (Wilson et al., 2007), changes in gene expression for inflammation (Cole et al., 2007), and negative affective states including depression (Cacioppo, Hughes, Waite, Hawkley, & Thisted., 2006; Weeks, Michela, Peplau, & Bragg, 1980). Loneliness is also linked to numerous health behaviors including medication non-adherence, physical inactivity, smoking, and increased health care utilization (Segrin & Passalacqua, 2010; Netz, Goldsmith, Shimony, Arnon, & Zeev, 2013; Shankar, McMunn, Banks, & Steptoe, 2011; Wilson & Moulton, 2010; Gerst-Emerson & Jayawardhana, 2015). With loneliness being viewed as amenable to change (Masi, Chen, Hawkley, & Cacioppo, 2010),

interventions reducing loneliness may also affect its related negative sequelae and improve health outcomes.

Qualitative research has shown that many PLWH experience profound loneliness and self-isolation due to fear of rejection and stigma (Audet, McGowan, Wallston, & Kipp, 2013; Signoracci et al., 2016), and some reports loneliness being more difficult than having an HIV diagnosis (Miles, Isler, Banks, Sengupta, & Corbie-Smith, 2011). A few studies that assessed the lived experiences of older PLWH showed that they often report isolation. In, particular, one study focusing on the health needs and concerns of women living with HIV/AIDS (age ≥40) found that the majority of the participants experienced rejection from family and friends and felt isolated (Enriquez, Lackey, & Witt, 2008). Many of these women indicated that HIV-related stigma was the main source of non-disclosure of their HIV status, which further heightened their feelings of isolation (Enriquez et al., 2008). Similarly, a qualitative study of older PLWH by Scrimshaw and Siegel (2003) also suggests that participants report loneliness due to past experiences of rejection by others and stigma associated with the disease. According to this study, the feelings of isolation became one of the many barriers in obtaining emotional and practical support as older PLWH age.

Given that loneliness is associated with a range of negative health outcomes in the general geriatric population and that loneliness may be significantly more pronounced among older PLWH due to factors associated with living with a highly stigmatizing condition, it is important to first understand the current knowledge about loneliness in older PLWH and the characterization of loneliness in terms of related factors. Moreover, with increased proportions of individuals aging with HIV/AIDS, the topic of loneliness may become more prevalent in the near future. A clearer understanding of loneliness in older PLWH is fundamental for identification of

possible gaps in the literature, provision of recommendations for future research, and development of interventions that target loneliness and its related factors. As such, the purpose of this review was to explore the current state of science regarding loneliness in older PLWH and to identify correlates of loneliness in older PLWH

Methods

This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009) and the Joanna Briggs Institute guidelines on systematic review (Aromataris & Pearson, 2014).

Search process and study selection

With the support of an experienced health science informationist, a comprehensive literature search was conducted using PubMed, PsycINFO, Embase, and CINAHL. The following key terms and concepts were combined using database-specific subject headings: *social isolation, loneliness, older adults, elderly, HIV, AIDS,* and *HIV/AIDS*. "Social isolation" was included in the key term to account for possible interchangeable terms (i.e., using social isolation to represent loneliness) used in studies and to capture research on loneliness comprehensively. Relevant references from the included publications were searched manually. The searches were limited to research on humans, English language publications, and original quantitative studies published between 2002-2018 that considered loneliness reported by older PLWH (defined as 50 years old or older based on literature and agency consensus) with or without an uninfected control group. This time period was selected based on the shift of the research in aging in HIV, where the research on social functioning in aging individuals with

HIV/AIDS started to expand and HIV infection began to emerge as a chronic and manageable disease rather than a life threatening condition (Justice, 2010). All searches were completed in April 2017 and updated in March 2018. Studies were only included if loneliness was measured with a validated questionnaire and if loneliness was assessed as an independent or dependent variable. Studies that utilized measures of objective social isolation (e.g., questions asking the number of frequent social contacts or the level of social participation), instead of loneliness, were excluded. Other exclusion criteria included: studies that focused on uninfected older adults or infected younger adults; studies focusing on countries other than Western Europe and United States due to possible ethnographic and cultural impact on the experience of loneliness; qualitative studies; and non-research articles without empirical findings and conference proceedings.

After removing duplicates of identified publications, titles and abstracts were screened by the first author under the supervision of a PhD prepared mentor. Full-text articles were reviewed if the title/abstracts met the eligibility for inclusion or if the title/abstracts did not provide enough information to determine eligibility for inclusion. Final relevant publications were reviewed thoroughly and the quality of the publications was independently appraised by two appraisers using the 8-item checklist from the Joanna Briggs Institute (Aromataris & Pearson, 2014; Joanna Briggs Institute, 2016) for evaluating cross-sectional studies. This checklist evaluates the quality of research studies, including the methods and analysis (**Table 2.1**). Quality assessment was evaluated using a 2-point system (0= "No", 1= "Yes") with possible total scores ranging from 0 (*lowest*) to 8 (*highest*) rating. Any scoring disagreements or concerns were discussed between the two appraisers and resolved by consensus.

Table 2.1. Critical Appraisal Checklist by Joanna Briggs Institute (Aromataris & Pearson, 2014)

1	Were the criteria for inclusion in the sample clearly defined?
2	Were the study subjects and the setting described in detail
3	Was the exposure measured in a valid and reliable way?
4	Were objective, standard criteria used for measurement of the condition?
5	Were confounding factors identified?
6	Were strategies to deal with confounding factors stated?
7	Were the outcomes measured in a valid and reliable way?
8	Was appropriate statistical analysis used?

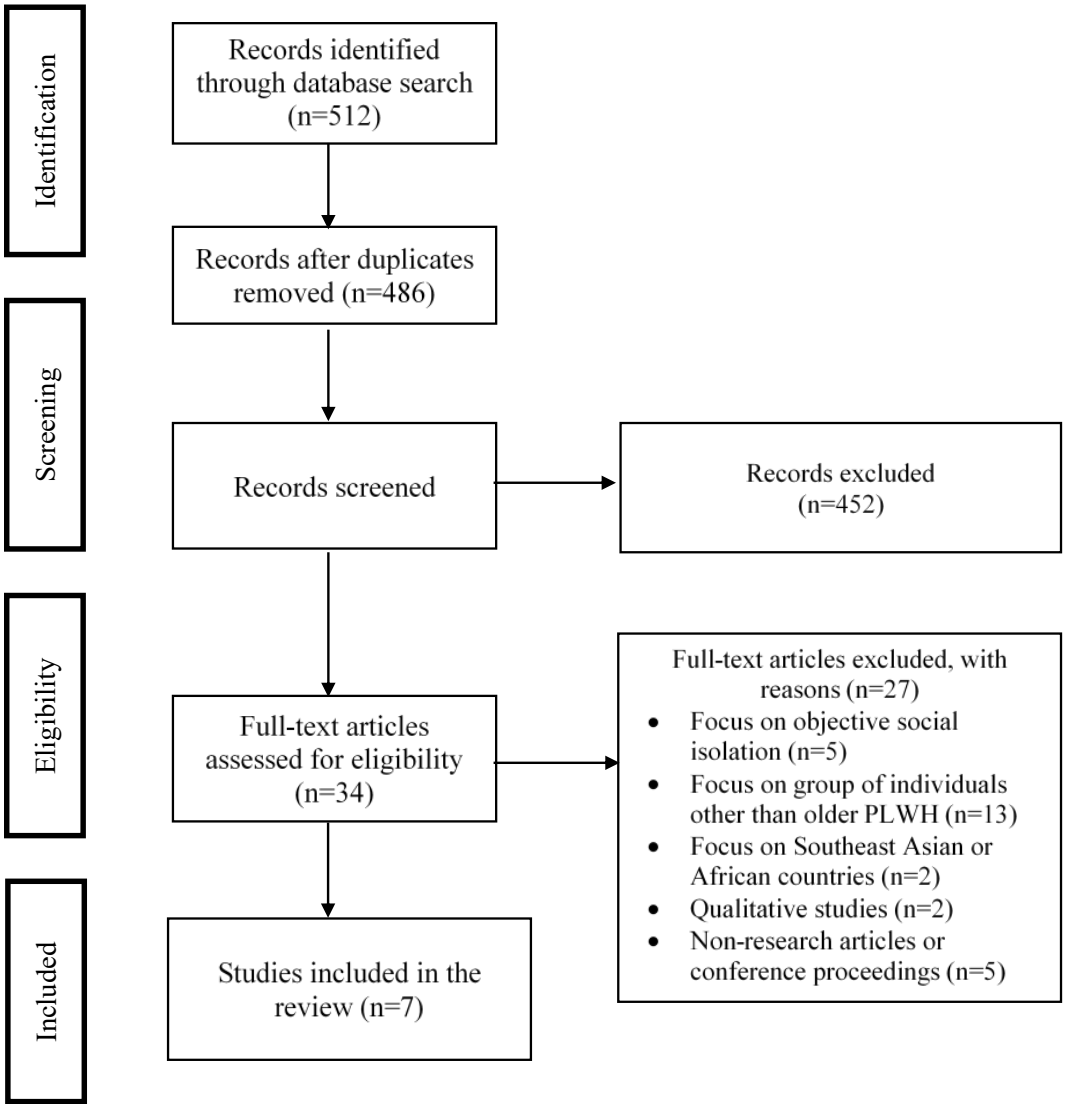
Results

Initially, a total of 512 publications were identified through database searches. Duplicates among the databases were removed, leaving 486 unique records. After screening the titles and abstracts for relevance based on the inclusion and exclusion criteria, the number of publications was reduced to 34. Twenty-seven articles were excluded during the full-text review, leaving seven publications that met all the eligibility criteria for inclusion in this review. **Figure 2.1** provides a flow diagram of search strategy and study selection for the current review according to the PRISMA framework (Moher, Liberati, Tetzlaff, & Altman, 2009).

Data from the selected articles were extracted into a summary matrix that included study design, aim, sample characteristics and setting, loneliness measure, the results of loneliness, and the quality assessment score of the study (**Appendix G: Table 2.2**). All of the studies were conducted in the United States. Of the seven studies, five involved secondary data analysis using larger datasets including Research on Older Adults with HIV (ROAH) Initiative (Golub et al.,

2010; Grov, Golub, Parsons, Brennan, & Karpiak, 2010; Siconolfi et al., 2013), the Silver Project (Greene et al., 2018), and the Research Core of Rush Center of Excellence on Disparities in HIV and Aging (CEDHA) cohort (Han et al., 2017).

Figure 2.1. PRISMA Flowchart of Study Selection.



ROAH was developed by the AIDS Community Research Initiative of America (ACRIA), a community-based HIV research and education agency based in New York City. Participants in ROAH were recruited through ACRIA's network of New York City-based AIDS service organizations. The final sample of ROAH is 914, and all are 50 years old or older. The Silver Project is a collaboration effort created by the San Francisco Department of Public Health to assess the needs of HIV-infected people who are 50 years old or older (Greene et al., 2018), and participants were recruited from two University of California San Francisco (UCSF)-affiliated HIV clinics. CEDHA is a collaborative effort between Rush University Medical Center and the Community Outreach Intervention Projects of the University of Illinois at Chicago and is a longitudinal cohort study of HIV-infected and uninfected people who are 50 years old or older.

Study sample sizes ranged from 96 to 914. Participants were mainly recruited from metropolitan/urban cities. The sample primarily consisted of non-Hispanic Whites or African Americans and male gender. Most studies (n=6) focused on older PLWH only (Golub et al., 2010; Greene et al., 2018; Grov et al., 2010; Mannes et al., 2017; Siconolfi et al., 2013; Vincent et al., 2017) with one study comparing older PLWH to older uninfected counterparts (Han et al., 2017).

Appraisal of the studies

Quality scoring using the checklist for evaluating cross-sectional studies indicated that studies reviewed had quality score of at least 5. Studies generally lacked on identifying confounding factors and ways to control for confounders. Studies utilizing secondary datasets did not provide the full information on the eligible criteria of study participants.

Measures of loneliness

The measures used to assess loneliness showed some consistency, with studies using validated tools including the University of California Los Angeles (UCLA) Loneliness Scale and the De Jong Geirveld Loneliness Scale.

Six of the studies used the UCLA Loneliness Scale. Developed by Russell, Peplau, and Ferguson (1978). The UCLA Loneliness Scale was designed to assess the subjective aspect of social isolation or loneliness; it assesses relational and social connectedness. The responses are rated on a Likert-type scale of 1 (*Never*) to 4 (*Often*). The UCLA Loneliness scale has four versions. The original version consists of 20 negatively worded items only (Russell, Peplau, & Ferguson, 1978). Later, a revised version incorporated 10 positively worded items and 10 negatively worded items (Russell, Peplau, & Cutrona, 1980). This revised scale has high internal consistency (Cronbach's alpha= 0.94) and discriminant validity. The total score ranges from 20 to 80 with higher scores indicating higher levels of loneliness. The third version of the UCLA loneliness scale (Russell, 1996) is an updated version from the revised version that reversed the content of one item and simplified the wording of three items (Russell, 1996). The number of items, total score, and range remained unchanged from the revised UCLA loneliness scale. The UCLA Loneliness Scale Version 3 has high internal consistency (Cronbach's alpha ranging from 0.89 to 0.94) and test-retest reliability over a one-year period (r=0.73). A short-form 8-item UCLA Loneliness Scale was developed by Hays and DiMatteo (1987). The responses are rated as 1 (*Never*) to 4 (*Often*) with total scores ranging from 8 to 32.

Our review found that among the six studies that used the UCLA Loneliness Scale, one study utilized the 8-item scale and categorized participants per predetermined cutoff points of 8-16 (*none*), 17-20 (*mild*), 21-24 (*moderate*), or 25-32 (*severe*) loneliness (Greene et al., 2018). Mannes et al. (2017) used the original 20-item scale and Vincent et al. (2017) used the revised

scale. The remainder of three studies used UCLA Loneliness Scale version 3 (Golub et al., 2010; Grov et al., 2010; Siconolfi et al., 2013).

The De Jong Gierveld Loneliness Scale was used in the study by Han et al. (2017). Originally, the 11-item De Jong Gierveld Loneliness Scale was developed using Weiss's definition of social and emotional loneliness; there are 6-items pertaining to emotional loneliness and 5-items related to social loneliness (De Jong Gierveld & Van Tilburg, 2010). This scale encompasses loneliness as a sense of emptiness and desire for social contacts, with the presence of people to rely on or trust and feel close to. The responses are rated dichotomously (0= "No", 1= "Yes") with total scores ranging from 0 (*absence of loneliness*) to 11 (*extreme loneliness*; De Jong Gierveld & Van Tilburg, 2010). Han et al. (2017) used the emotional loneliness subscale only and made modifications to this subscale by asking participants to respond using a 5-point Likert scale, combining two similar items, and making word changes for better comprehension. They used the following items: "I experience a general sense of emptiness," "I miss having people around," "I feel like I don't have enough friends," "I often feel abandoned," and "I miss having a really good friend." In comparison to the original scoring, Han et al. (2017) averaged the summed scores, to make the scores range from 1 to 5 as is in the original emotional loneliness subscale, with higher scores indicating greater loneliness.

Although all the included studies used validated measures for loneliness, only a few reported the average score, only one study reported loneliness in terms of severity levels (Greene et al., 2018), and there was variability in the measures used (e.g., different measures or versions), making it challenging to directly assess and compare the severity of loneliness across studies. Additionally, these scales did not have cut-off points except for the short form 8-item UCLA Loneliness Scale (Greene et al., 2018). In the study by Greene and her colleagues (2017), the

predefined cut points were determined by conversation with the original developers of the scale. Based on the cutoff, this study showed that 58% of participants reported being lonely, with 24% reporting mild, 22% reporting moderate, and 12% reporting severe loneliness.

Factors associated with loneliness

Age correlated with higher loneliness in one study. Golub et al. (2010) found that being over the age of 60 was associated with a higher average score of loneliness in a multivariate analysis, but the effect size and *p-value* were not reported. Similar to this finding, Mannes et al. (2017) showed that those over the age of 60 had a higher score on loneliness than those who were younger (50 to 59 years old), but this difference was statistically non-significant (p=.751).

Race/ethnicity was related to loneliness in some studies. African American (AA)/Black adults reported significantly lower scores on loneliness than White adults (Han et al., 2017) and Latinos (Siconolfi et al., 2013). Han et al. (2017) compared the differences in loneliness based on race (AA vs. White) in both HIV-infected and uninfected older adults. They found that AA participants report significantly lower overall levels of loneliness than White participants, regardless of HIV status, controlling for covariates and confounders (β=-0.39, p<.01). Siconolfi et al. (2013) found that greater loneliness was indicated among Latino participants compared to AA/Black or White participants (F=3.81, p=.01).

In addition to the effect of race/ethnicity on loneliness, sexual orientation and gender were also related to loneliness in two studies. Siconolfi et al. (2013) further explored whether sexual orientation and gender were related to loneliness and found that heterosexual men reported higher loneliness than heterosexual women and gay/bisexual men (F=7.01, p=.001). Gay/bisexual men had higher loneliness than heterosexual women but this difference was not

statistically significant (Siconolfi et al., 2013). Similar to these findings, Vincent et al. (2017) also found that men (heterosexual men and MSM) had higher loneliness than women (p=.031).

Vincent et al. (2017) examined the association between HIV-related shame and three dimensions of health-related quality of life (HRQoL) using structural equation modeling and evaluated whether there was any indirect effect of loneliness. The study showed that HIV-related shame accounted for at least 29% of variance in loneliness in their sample of 299 older PLWH and that the association between HIV-related shame and social well-being (one of the dimensions of HRQoL) was partially mediated by loneliness. Specifically, when this analysis was stratified by gender (men vs. women), the results revealed that the association between HIV-related shame and social well-being was fully mediated by loneliness in men only, whereas this association was partially mediated by loneliness in women. The findings suggest that there may be gender differences in how loneliness affects outcomes.

Two studies found that loneliness is linked to risky behaviors, including unprotected sex (Golub et al., 2010) and substance use (Greene et al., 2018). Golub et al. (2010) used the ROAH dataset for their data analysis and found that unprotected anal/vaginal sex in the past 3 months was associated with greater loneliness (odds ratio [OR], 1.03; 95% CI,1.01-1.06, p<.01). Using the chi-square test, Greene et al. (2017) found that lonely participants were more likely to be at risk for problematic use of alcohol and tobacco products (p=.001) and to be a current cigarette smoker (p=.04) compared to non-lonely participants. On the contrary, one study found no association between substance use (cigarette, alcohol, marijuana, popper, and hard drug use) and loneliness (Siconolfi et al., 2013).

Two studies suggest that loneliness is associated with depressive symptoms (Grov et al., 2010; Greene et al., 2018). Grov et al. (2010) found in their stepwise logistic regression model

that higher rates of loneliness (OR, 1.06; 95% CI, 1.04-1.09; $p<.001$) and HIV-related stigma place older PLWH at an increased risk for major depressive symptoms (using the Center for Epidemiological Studies Depression Scale; CES-D cut-point for major depression of ≥ 23) controlling for demographic (gender, sexual orientation, age) and clinical (functional status, subjective cognitive function, AIDS diagnosis, CD4+ T cell count) factors. This finding aligns with the results of Greene et al. (2017), which showed more depressive symptoms (Patient Health Questionnaire; PHQ-9 ≥ 5) in lonely participants compared to the participants who are not lonely ($p <.001$).

Some health outcomes were related to loneliness in two studies, namely HRQoL, functional status, and cognitive function. Greene et al. (2017) found, in unadjusted models, that loneliness was associated with reduced HRQoL (Prevalence ratio [PR], 1.36; 95% CI, 1.13-1.63) and poor functional status (PR, 1.19; 95% CI, 1.01-1.40). When other covariates were included, however, the loneliness was no longer statistically significant and only depressive symptoms and annual income were the main factors related to HRQoL and functional status (Greene et al., 2018). Cognitive function was associated with loneliness in a study comparing HIV-infected older adults to their uninfected counterparts (Han et al., 2017). Han et al. (2017) demonstrated an interaction between AA/Black race and loneliness on the global score of objective cognitive function among HIV-infected participants but not among uninfected participants. In AA/Black adults with HIV, greater loneliness was associated with lower objective cognitive function (Han et al., 2017). Their correlational analysis also found a weak but significant correlation between loneliness and global functioning on cognitive test batteries (r=-.24; p=.007) among AA/Black older PLWH but not among their HIV-infected White counterparts (Han et al., 2017).

Discussion

This review examined quantitative studies assessing loneliness in older PLWH. There was overlap in the datasets that some studies utilized. The UCLA Loneliness Scale and the de Jong Gierveld Loneliness scale were the two measures used to assess loneliness in the reviewed articles. However, there was variability in the versions of the UCLA scale, making it challenging to directly compare the severity of loneliness across the studies. Additionally, a study comparing the UCLA Loneliness Scale and the de Jong Gierveld Loneliness scale suggests that the de Jong Gierveld Loneliness scale is relatively superior for assessing loneliness in the study of middle-aged and older adults due to problems in item wording in the UCLA Loneliness Scale (Penning, Liu, & Chou, 2014). However, only one out of seven selected studies used the de Jong Gierveld Loneliness scale, and more empirical data are needed to determine its potential superiority over the UCLA Loneliness Scale in predicting loneliness among older PLWH.

The American Association of Retired Persons (AARP) conducted a national survey of 3,012 middle-aged to older (45 years old or older) Americans to assess loneliness and characterize those who are lonely. AARP found that at least 35% of older Americans were categorized as lonely (UCLA Loneliness Scale score $\geq$44, cutoff designated by the AARP) and loneliness was a significant factor related to self-rated health (Wilson & Moulton, 2010). Although severity or prevalence estimates of loneliness in older PLWH were difficult to determine due to the variability in the measures across the studies, it was clear that they, like the general older adult population, experience at least some levels of loneliness. Also, while some studies included in this review reported low average loneliness scores, studies that utilized Silver Project and ROAH datasets had higher mean scores of loneliness than the studies that utilized other datasets (Mannes et al., 2017; Vincent et al., 2017) or the reported average loneliness score

from the AARP survey (40.4 for males and 39.2 for females on UCLA Loneliness Scale). For example, a study using the Silver Project dataset (Greene et al., 2018) showed that about 58% of older PLWH in their sample reported being lonely, which is considerably larger than in the general older adult population. Studies using the ROAH dataset (Grov et al., 2010; Siconolfi et al., 2013) had a mean score of loneliness of 43.9 for all sample, 41.5 for heterosexual women, and 44.9 for heterosexual men. Different versions of measures and different sample characteristics may help explain these disparate findings.

One possible explanation for the considerably lower score of loneliness shown in some studies (Mannes et al., 2017; Vincent et al., 2017) may be due to the survivorship effect. Older age is particularly susceptible to the changes that naturally occur with aging that are closely tied to social isolation and loneliness, such as retirement, disability, and bereavement (Bekhet & Zauszniewski, 2012). Long-term survivors of HIV infection might have faced these changes early on and possibly accumulated more challenges and stressors that occur with aging (e.g., comorbidities). But due to the survivorship effect, older PLWH with chronic HIV infection might have developed adequate coping strategies to overcome the challenges associated with natural aging changes and social transitions, which may have resulted in the reduced feelings of loneliness. Reasons for high levels of loneliness shown in some studies (Green et al., 2017; Grov et al., 2010; Siconolfi et al., 2013) may be related to the layered stigma related to older age and HIV (Emlet, 2006) along with the changes that come with aging, which may accentuate the feelings of loneliness. However, included studies in this review did not assessed the effects of chronicity of HIV on loneliness and thus this hypothesis needs to be tested in future studies to have a clearer understanding of the possible survivorship effects on loneliness.

Sociodemographic correlates of loneliness were similar to those in uninfected older adults. Older age was related to loneliness in some studies (Golub et al., 2010; Mannes et al., 2017), which parallels existing research in general older adult population (Cohen-Mansfield, Hazan, Lerman, & Shalom, 2016). Participants who self-identify as White race and/or Latino ethnicity were more likely to be lonely than AA/Black participants (Han et al., 2017, Siconolfi et al., 2013). Some studies in this review reported a higher average loneliness score among men than women (Siconolfi et al., 2013; Vincent et al., 2017). Studies among the general population of older adults show similar findings—men tend to report greater loneliness than women (Wilson & Moulton, 2010) but women are more often categorized as lonely than men (Cohen-Mansfield et al., 2016; Fisher et al., 2014). Further research is needed to empirically test possible gender differences in the levels and experiences of loneliness among older PLWH.

HIV-related shame or stigma had a significant association with loneliness (Vincent et al., 2017). A recent review on social networks of older PLWH suggests that older PLWH have limited and tenuous social connections due to their highly stigmatized disease and fear of rejection when HIV status is disclosed (Gannon & Stacciarini, 2016). More research is needed to examine the associations among HIV-related stigma and loneliness to better understand unique predictors that may serve as targets to reduce loneliness in older PLWH.

Loneliness has been linked to many health behaviors in the general population, including medication non-adherence (Segrin & Passalacqua, 2010), sedentary lifestyle (Netz, Goldsmith, Shimony, Arnon, & Zeev, 2013), and smoking (Shankar, McMunn, Banks, & Steptoe, 2011; Wilson & Moulton, 2010). Our review also indicates that loneliness is related to health behaviors, including substance use (Greene et al., 2018) and unprotected sex (Golub et al., 2010). However one study did not find a significant association between substance use and loneliness

(Siconolfi et al., 2013). The contrasting findings might be due to the different ways in which these studies assessed substance use. The former utilized a screening tool to identify problematic substance use behaviors (Greene et al., 2018), whereas the latter used a self-report of substance use in the past 3 months (yes or no; Siconolfi et al., 2013). Furthermore, while Greene et al. (2018) dichotomized participants into two categories (lonely versus not lonely) based on the score of loneliness and treated loneliness as a categorical variable, Siconolfi et al. (2013) analyzed loneliness as a continuous variable (Siconolfi et al., 2013).

This review found that loneliness was associated with some clinical outcomes including cognitive function (Han et al., 2017), depressive symptoms (Grov et al., 2017; Greene et al., 2018), quality of life (Vincent et al., 2017; Greene et al., 2018), and functional impairment (Greene et al., 2018) in older PLWH. The link between cognitive decline and loneliness has been well documented in the general older adult literature (Ellwardt, Aartsen, Deeg, & Steverink, 2013; Holwerda et al., 2014; Wilson et al., 2007). Some studies suggest that loneliness may be a marker of psychosocial stress that promotes inflammation and affects brain function (Donovan et al., 2016). Although uninfected older adults are less likely to report depressive symptoms, the opposite is true with the HIV infected older adults. Depression has long been associated with numerous adverse outcomes and is a common comorbid condition among older PLWH. Depression is closely tied to loneliness but is a distinct concept as evidenced by studies that showed predictability of loneliness on depression but not depression on loneliness. For example, a mixed methods study describing the experience of depression among uninfected older adults showed that many older persons reported loneliness as a unique proximal factor that precedes depression (Barg et al., 2006). Similarly, Cacioppo, Hawkley, and Thisted (2010), using cross-lag path analyses, found that loneliness predicted changes in depressive symptoms but not vice

versa in middle aged and older adults. A longitudinal study is warranted to assess the predictability of loneliness to depression, and to determine whether targeting loneliness would help with alleviating or preventing depression in older PLWH.

There were several gaps and challenges in research in loneliness in older PLWH. First, quantification of the severity of loneliness has been a challenge in research due to inconsistencies in the conceptual definitions of social isolation, loneliness, and living alone (Perissinotto & Covinsky, 2014). Some researchers combined measures of social isolation (i.e., objectively quantifiable social contacts/activity) to define loneliness (these studies were excluded). A clear definition of loneliness is essential to future research, as this concept is closely related to many other concepts but is distinct. More qualitative research unraveling the experience of loneliness in older PLWH is warranted. Furthermore, unlike scales used to assess symptoms of depression, validated loneliness scales lack cutoff points and present loneliness in relative terms such as "higher score indicating more loneliness." The extent to which the levels of loneliness signal the need for interventions or whether a certain score of loneliness has a clinical implication are areas of further research. Secondly, loneliness is often related to depression, shifting the focus of loneliness more to depression rather than loneliness itself. The overlapping manifestations of loneliness and depression often allow clinicians and researchers to focus more on depression, when loneliness might be the key risk factor leading to depression. Thirdly, all of the studies in this review are cross-sectional in nature, providing no information on the direction of the association between loneliness and other variables. Evidence is lacking on the transient versus persistent feelings of loneliness and their effects on health in older PLWH. The feelings of loneliness can be a fleeting emotion or it may persist chronically, affecting the lives of older PLWH. The extent to which chronicity of loneliness has an impact on clinical outcomes among

older PLWH needs to be investigated. Additionally, functional decline and illness can influence individuals to socialize less, leading to isolation and loneliness. Alternatively, loneliness may also be a causal factor for functional decline or illness. Prospective longitudinal research may help clarify the independent effect of loneliness on health and how it drives health in older PLWH. Finally, given its association with factors contributing to negative health outcomes in older PLWH, loneliness may be a promising target for interventional research.

Clinical Implications

In older PLWH, HIV is a complex disease that is associated with not only multi-morbidities and syndromes, but also psychosocial challenges. Understanding loneliness as a unique phenomenon that may have an impact on the health of aging individuals with HIV is imperative. While it is difficult to quantify the degree or level of loneliness that would meaningfully affect health outcomes, it influences patient well-being. Nurses working in HIV practice are on the forefront of patient symptom management and identification of psychosocial needs, and therefore it is important for nurses to comprehensively assess psychosocial issues including loneliness and the need for psychosocial resources among older patients living with HIV. Nurses are in key positions to identify whether older patients with HIV are socially isolated and to ask if loneliness has any effect on their lives. There is an easily administered tool available for clinicians to screen for loneliness in the clinical setting (Hughes, Waite, Hawkley, & Cacioppo, 2004), which may be helpful in identifying loneliness so that a nursing care plan can mitigate its negative effects.

Studies in the general older adult population and some studies with older PLWH, included in this review, show that loneliness is closely related to depression and cognitive

decline. Intervening to reduce loneliness may therefore prevent depression and cognitive decline but more longitudinal research is needed to evaluate the effects of loneliness in health outcomes and to develop interventions to cope with loneliness among older PLWH.

Limitations

There are several limitations to this review. This review did not include grey literature including conference proceedings, doctoral dissertations, or master's theses. Therefore, it may have not located recent studies/findings on loneliness in older PLWH that are in process for publication. A few relevant studies conducted among older PLWH in Africa, South Asian countries, and South America have been excluded from this review due to variability in ethnography and the experience of loneliness. The keywords used to identify and retrieve publications may have not been sufficiently inclusive. Older individuals with newly acquired HIV infection may have different experiences in relation to social relationships and feelings of loneliness compared to those who may have lived with the infection for a longer duration of time. Yet, no studies have investigated whether there is an indication that the feelings of loneliness is affected with the number of years of HIV diagnosis. Lastly, loneliness was assessed using different versions or types of measures across studies, making it difficult to synthesize some of the results. The heterogeneity of the measures utilized in the study do not allow for cross-study analyses. Despite these limitations, this review adds to the HIV and aging literature on the topic of loneliness in older PLWH by exploring the current state of knowledge in loneliness and identifying the related factors of this understudied phenomenon in older PLWH.

Conclusions

Loneliness is a common problem among older PLWH. Research on the psychosocial context of older PLWH has increased recently and loneliness is deemed an important factor that may affect the health and lives of older PLWH. Our review suggests that loneliness is related to sociodemographic factors including age, race/ethnicity, gender/sexual orientation, HIV-related stigma, risky behaviors, and clinical outcomes. The review found that current studies on loneliness in older PLWH are descriptive in nature. Considering the potential for preventing some clinical outcomes related to loneliness, screening for loneliness in clinic settings may be beneficial. Additional qualitative, quantitative, and mixed-methods studies are needed to broaden our current knowledge of loneliness in this population. Future studies should also consider investigating the association between living arrangements and loneliness, such as geographic arrangements including rural or urban environments, and living environments like nursing homes, residential homes, or half-way houses. Longitudinal research on loneliness among older PLWH is warranted to investigate the temporal effects of loneliness as well as to examine potential mechanisms and causal pathways that link loneliness and how it drives the health of older PLWH. Moreover, loneliness needs to be addressed simultaneously with objective isolation to disentangle the associations among both aspects of social isolation and health.

Key Considerations

- Older persons living with HIV may face challenges that may affect their social lives, including life course transition, ageism, and HIV-related stigma, which all may escalate the feelings of loneliness and affect their overall quality of life and well-being.
- Loneliness is related to clinical outcomes in older persons living with HIV, including depression, cognitive function, quality of life, and functional status.
- Targeting loneliness and its associated factors may be beneficial in preventing depression and/or cognitive decline and improve well-being.

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Note. References marked with one asterisk(*) indicate studies included in the systematic review.

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CHAPTER 3

DETERMINANTS OF LONELINESS IN OLDER PERSONS LIVING WITH HIV/AIDS

Abstract

Introduction: Loneliness poses a significant risk for morbidity and mortality in the context of older adulthood. Research shows that older persons living with HIV (PLWH) often face increased and complex vulnerability in terms of physical and psychosocial needs which may promote loneliness. However, there remains a dearth of information on the risk factors for loneliness in older PLWH. The current study sought to identify correlates of loneliness.

Methods: A sample of 146 older PLWH (age ≥50) was recruited from a comprehensive HIV care clinic in the Southeastern region of the United States. Participants completed a battery of questionnaires on loneliness, depression, HIV-related stigma, social network size, HIV-disclosure status, comorbidities, functional status, and demographics. Clinical data including viral load and CD4+ T cell count were abstracted from their electronic health records.

Results: Participants were predominantly male (60%) and African American (86%). The mean (standard deviation) age was 56 (4.55). Twelve percent (n=17) reported past history of homelessness. More than 41% of our sample was categorized as lonely. Multivariable modeling revealed that depression and HIV-related stigma explained 41% of the variance in loneliness, above and beyond the effects of demographics, functional status, and comorbidities (R^2=0.41, F(7, 138)=13.76, p<0.001).

Discussion: The current study underscores the importance of targeting HIV-related stigma and depression to potentially reduce loneliness and improve well-being of this ever-growing sample of older adults. Greater understanding of the mechanisms by which loneliness affects health among older PLWH could help better inform efforts to improve health in this patient population.

DETERMINANTS OF LONELINESS IN OLDER PERSONS LIVING WITH HIV/AIDS

Introduction

Loneliness is an aversive emotional experience that results from a perceived discrepancy between one's desired and actual intimate and social support (e.g., low quality, emotionally distant, unsatisfying; Peplau & Perlman, 1982). Loneliness appears to be highly prevalent among the general geriatric population with as many as 35% to 40% of older adults reporting feelings of loneliness (Theeke, 2009; Golden et al., 2009; Routasalo, Savikko, Tilvis, Strandberg, & Pitkala, 2006; Savikko, Routasalo, Tilvis, Strandberg, & Pitkala, 2005; Wilson & Moulton, 2010). These estimates are concerning because loneliness poses a significant risk for morbidity and mortality in the context of older adulthood (Cornwell & Waite, 2009) and is linked to many negative health outcomes. For example, loneliness has been associated with elevated blood pressure in both cross-sectional and longitudinal studies (Hawkley, Masi, Berry, & Cacioppo, 2006; Hawkley, Thisted, Masi, & Cacioppo, 2010), increased risk for cognitive decline and Alzheimer's disease (Wilson et al., 2007), changes in gene expression for inflammation (Cole et al., 2007), and negative affective states (Cacioppo, Hughes, Waite, Hawkley, & Thisted, 2006; Weeks, Michela, Peplau, & Bragg, 1980).

The clinical and research implications of loneliness for older persons living with HIV (PLWH; age 50 years old or older) are becoming more relevant in the United States with the rise in the number of older PLWH due in part to the advancements in and access to antiretroviral therapy (ART) and HIV care services that have prolonged the life expectancy of people living with HIV/AIDS (PLWH). Although HIV incidence rates among those aged 50 and older in the United States have decreased from 2011 to 2015, an estimated 17% of new HIV diagnoses in 2016 occurred in this age group (Centers for Disease Control and Prevention [CDC], 2016).

Furthermore, there is an increased HIV prevalence rates among this age group; an estimated 47% of PLWH in the United States in 2015 were 50 years old or older (CDC, 2016) and this number is projected to grow to 70% by 2020 (Brooks, Buchacz, Gebo, & Mermin, 2012).

Research shows that older PLWH often face increased and complex vulnerability in terms of physical and psychosocial needs, which may promote loneliness. Recent studies suggest that PLWH may be more vulnerable to early onset of aging, such that they often exhibit higher numbers of age-associated comorbidities such as cardiovascular diseases or diabetes at a much younger age than their uninfected counterparts (Pathai, Bajillan, Landay, & High, 2014; Guaraldi et al., 2011), indicating that older PLWH may experience a greater physical burden. Health disparities in older PLWH are also reflected in depression, with older PLWH commonly reporting depressive symptoms whereas uninfected older adults are less likely to report depression (Greene et al., 2015; Havlik, Brennan, & Karpiak, 2011). Studies also indicate that older PLWH tend to live alone and have limited and inadequate social networks compared to their younger counterparts (Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005a). These health and psychosocial concerns may further heighten the feelings of loneliness in this subpopulation of older adults.

To our knowledge, only two studies have investigated the effects of loneliness on health outcomes with older PLWH, and these studies suggest that loneliness affects quality of life, functional status, and cognitive function (Greene et al., 2018; Han et al., 2017). Greene and colleagues (2017) have shown that loneliness was linked to functional status and health-related quality of life. Han et al. (2017), in a secondary data analysis, compared their sample of older PLWH (mean age=58.79) to their uninfected counterparts. Although African American (AA) participants reported less loneliness than white participants, findings indicated an interaction

between race and loneliness on objective cognitive function, such that those AAs reporting greater loneliness were more likely to have objectively measured cognitive impairment (Han et al., 2017). Despite these important studies suggesting the effects of loneliness on health outcomes, there remains a dearth of information on the risk factors of loneliness in older PLWH. Since loneliness is potentially modifiable (Masi, Chen, Hawkley, & Cacioppo, 2011), identification of determinants of loneliness may reveal possible intervention targets to reduce loneliness and the related negative health sequelae experienced by older PLWH.

Loneliness may be particularly severe for older PLWH, especially as they experience reduced social network size for various reasons including age-related changes (reduced functionality, deaths of peers, empty nest), HIV-related stigma and discrimination, and self-protective withdrawal from society (Emlet, 2006; Rabkin, McElhiney, & Ferrando, 2004; Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005a; Shippy & Karpiak, 2005b). HIV infection has long been associated with stigma that often affects those who are socially disenfranchised and excluded (Emlet, 2006). Studies indicate that HIV-related stigma is associated with loneliness in older PLWH (Golub et al., 2010; Grov, Golub, Parsons, Brennan, & Karpiak, 2010; Mannes, Burrell, Dunne, Hearn, & Whitehead, 2017; Siconolfi et al., 2013). Aging with HIV has been reported as more stigmatizing because older age is related to ageism, which is associated with negative stereotypes like incompetence and frailty (Emlet, 2006). Ageism may present as a layered stigma in addition to the pre-existing HIV-related stigma and may further exacerbate the feelings of loneliness. These stigmas can lead to feelings of shame, difficulty reaching out to others, and "silencing" HIV status because of fear of rejection, which may increase a sense of loneliness, promote self-protective withdrawal, limit much needed support from others, and ultimately jeopardize one's health. Some qualitative research has shown

that PLWH experience loneliness and self-isolation due to fear of rejection and internalized stigma (Audet, McGowan, Wallston, & Kipp, 2013; Signoracci et al., 2016) and that HIV-related stigma serves as the main source of non-disclosure of their HIV status which accentuates loneliness (Enriquez, Lackey, & Witt, 2008). Despite qualitative evidence for the associations among stigma, HIV disclosure status, and loneliness, no study has quantitatively evaluated such associations. In order to determine the ideal target for intervention or prevention of loneliness, it is important to assess which factors are related and to what extent they are related to loneliness

Studies with uninfected older adults suggest a number of predictors of loneliness. Hawkley et al. (2008) used a conceptual framework of social networks (Berkman, Glass, Brissette, and Seeman, 2000) to examine factors related to loneliness in a sample of 225 uninfected middle-aged and older adults living in the United States and found that demographic factors (age, gender, race/ethnicity), functional status, and social network size (assessed by the quantity of social contacts and level of participation in social activities) explained about 37% of the variance in loneliness (Hawkley et al., 2008). This was similar to the results of other studies in uninfected older adults (Cohen-Mansfield & Parpura-Gill, 2007; Theeke, 2009).

The current study sought to identify determinants of loneliness in a sample of older PLWH. Specifically, we examined the relationships of HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size to loneliness while controlling for significant demographic factors, functional status, and comorbidity burden. We controlled for functional status and comorbidities because being functionally impaired and having multimorbidities may hinder an older individual's engagement in social activities and may contribute to feelings of loneliness (Greene et al., 2018; Pinquart & Sorensen, 2001). Based on

the literature, we hypothesized that HIV-related stigma, HIV disclosure status, depression, and social network size would all be associated with loneliness.

Methods

Participants & Setting

This study employed a cross-sectional design. A sample of HIV-infected older adults enrolled at a large comprehensive metropolitan HIV care clinic located in the southeast region of the United States, was recruited through flyers, word of mouth, and healthcare provider referrals from August 2016 to April 2017. Eligible individuals were 50 years old or older, living with HIV, and had at least one medical visit established in the recruiting clinic. Due to the likelihood of low literacy in this population, information about informed consent was provided to eligible individuals with ample time for questions. A consent post-test was given to assess individual's capacity to provide informed consent and understanding of the content prior to obtainment of informed consent and enrollment into the study. Individuals who failed the consent post-test after three attempts were excluded (n=3).

Data Collection

Approval for the study protocol was granted from the university's institutional review board (IRB), the affiliated-hospital's Research Oversight Committee, and the clinic's Research Committee prior to study enrollment. The PI discussed the study with individuals who were interested in the study and established study eligibility for those with continued interest. After prescreening and provision of informed consent, eligibility criteria were confirmed by review of the electronic medical records (EMR). Participants then completed a baseline study survey via

Research Electronic Data Capture (REDCap) on a computer. REDCap is a secure, web-based, electronic data capture tool allowing online survey entry (Harris et al., 2009) in compliance with the university's IRB HIPAA policies and procedures. All participants were first shown how to use the mouse/computer and provided with sample questions for practice. Total time to complete the survey was approximately 45-60 minutes. Potential risks of the study were minimal but included the possibility of distress and fatigue during or after the questionnaire administration. To reduce distress and fatigue, participants were given time to rest or to use the restroom anytime during the study survey. Participants received $25 in cash upon completion of the study survey for their participation. HIV biomarker data were collected from EMR.

Measures

Comorbidity burden was measured using the self-reported version of the Charlson Comorbidity Index (CCI) (Charlson, Pompei, Ales, & MacKenzie, 1987). The CCI includes 19 conditions in which participants were asked to identify (Yes/No) the conditions that they were diagnosed. These conditions included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, gastrointestinal disease, mild and serious liver disease, uncomplicated and complicated diabetes mellitus, hemiplegia, moderate and severe renal disease, cancer, leukemia, lymphoma, and secondary metastasis. The comorbidities were assigned a weight based on the adjusted 1-year mortality risk (Charlson et al., 1987). AIDS diagnosis was omitted from the CCI in our study as its weight is outdated in the current era of combination antiretroviral therapy (Zavascki & Fuchs, 2007) and age was not adjusted in this study as our sample consisted only of those who are aged 50 years old or older. The CCI has strong construct validity and reliability

(Hall, 2006) and has been used in previous studies with PLWH (Lohse et al., 2011; Rodriguez-Penney et al., 2013).

Functional Status was measured using a modified version of Lawton and Brody's Instrumental Activities of Daily Living Scale (IADL; Lawton & Brody, 1969), which consists of self-reported levels of functionality on eight daily tasks (e.g., using the telephone, shopping, preparing meals, doing housework, doing laundry, traveling methods, medication management, and managing finances) with possible scores ranging from 0 (low function, dependent) to 8 (high function, independent). IADL is also used as an indicator of the severity of chronic illness and to evaluate whether the skills needed to live independently are present in an individual. The IADL has been used frequently in HIV research and shows good reliability (α= .85) and validity.

HIV-related stigma was measured with Kalichman et al.'s Internalized AIDS-Related Stigma Scale (Kalichman et al., 2009), which contains 6 items rated dichotomously (1=agree, 0=disagree), with scores ranging from 0 to 6. Questions include: "It is difficult to tell people about my HIV infection"; "being HIV positive makes me feel dirty"; "I feel guilty that I am HIV positive"; "I am ashamed that I am HIV positive"; "I sometimes feel worthless because I am HIV positive"; and "I hide my HIV status from others". A higher score is indicative of greater HIV-related stigma. This scale shows good internal reliability (α= .73 to .76) and criterion validity. The Cronbach's alpha for our sample was 0.83.

HIV-disclosure status was assessed using one-item that assessed whether participants disclosed their HIV status to someone. Participants were dichotomized into two groups based on their response (0=disclosure to no one, 1=disclosure to someone). The question was adapted from the Disclosure Risk form (Huba, Melchior, Staff of the Measurement Group, & Washington University HRSA SPNS Cooperative Agreement Project, 1996).

Depressive symptoms were assessed using the 20-item Center for Epidemiologic Studies Depression Scale Revised (CESD-R; Eaton, Smith, Ybarra, Muntaner, & Tien, 2004) that assesses nine symptoms of depression (dysphoria, anhedonia, appetite, sleep, concentration, worthlessness, fatigue, agitation, and suicidal ideation) in accordance with the Diagnostic and Statistical Manual (DSM-V) diagnostic criteria for Major Depressive Disorder. Participants answer 0= "Not at all or less than one day" to 3= "Nearly every day for 2 weeks," with possible scores ranging from 0 to 60. A score $\geq$ 16 indicates at risk for clinical depression. The scale has good validity and internal consistency (Van Dam & Earleywine, 2011) and the Cronbach's α was 0.93 in our sample.

Social network size was measured using the Social Network Index (SNI), which assesses social contact with or participation in 12 types of social relationships at least once every 2 weeks in person or on the phone (Bickart, Wright, Dautoff, Dickerson, & Barrett, 2011; Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997) The types of social relationships include relationships with a spouse, parents, parents-in-law, children, other close family members, close neighbors, friends, colleagues/coworkers, schoolmates, fellow volunteers, members of groups without religious affiliation, and members of religious groups (Cohen et al., 1997). The total number of people with whom the participants have regular contact was summed across the 12 possible social relationships, reflecting the *overall social network size*. A higher score indicates greater social network size. SNI was utilized on a sample of older adults in a number of studies (Bickart et al., 2011; Cohen et al., 1997).

Loneliness was measured with the Patient-Reported Outcomes Measurement Information System (PROMIS)-Social Isolation (SI) Short Form 8a. The PROMIS measures are normed using the general United States population and are standardized based on common metrics that

allow for comparisons across domains and chronic diseases (Cella et al., 2010). The normative sample used for PROMIS-SI scale included individuals with chronic illnesses (PROMIS, 2015). The PROMIS-SI instrument uses 8-items to assess *perceptions* of being avoided, excluded, detached, disconnected from, or unknown by others on a 5-point Likert scale (1=Never to 5= Always; PROMIS, 2015). A total raw score ranging from 8 to 40 is calculated by summing the values of the response to each item. The total raw score of each participant was converted into a standardized T-score metric with a mean of 50 and a standard deviation (SD) of 10 (Cella et al., 2010), following the score conversion table in the scoring instruction (PROMIS, 2015). Hence, a T-score of 50 represents an average score and a T-score of 60 represents one SD higher score of loneliness than the average persons with chronic illnesses in the United States (PROMIS, 2015). Based on the cutoff score of PROMIS-SI scale used in previous studies (Karayannis, Baumann, Sturgeon, Melloh, & Mackey, 2018), participants were categorized as lonely (T-score 50-100) and not lonely (T-score <50). Cronbach's alpha for our sample was 0.95.

Covariates and demographic characteristics

We collected demographic data on age, gender, sexual orientation, years since HIV diagnosis, highest level of education, race/ethnicity, monthly income, and having a history of homelessness in the past 12 months via self-report to control for potential covariates and to describe and characterize the sample. History of homelessness in the past 12 months was assessed by a question, "In the past 12 months, have you been homeless at any time? By homeless, I mean you were living on the street, in a shelter, a Single Room Occupancy hotel, temporarily staying with friends/family, or living in a car." HIV markers including CD4+ T cell count and viral load were abstracted from EMR. The lab values reported within the closest time

from baseline study visit were selected, not to exceed two months (i.e., the lab reports selected were ±2 months from the baseline visit). Undetectable viral load was reported EMR lab value less than 40 copies/mL.

Data Analysis

All statistical analyses were performed with SPSS version 24 (IBM Corp, Armonk, NY). Univariate descriptive statistics were calculated for demographic and study variables. All continuous data are represented as a mean (SD); all categorical data are presented as frequencies (percentages). Bivariate relationships between study variables, demographic factors, and loneliness were assessed using Pearson correlations and ANOVA, as appropriate. Demographic factors that showed association with loneliness in bivariate analysis with $p<.10$ were identified as covariates and retained in the first step of subsequent multiple linear regression analysis. The variables were entered sequentially with non-modifiable factors in the first step and modifiable factors (study variables) in the second step. Violations of key assumptions for multiple linear regression, including linearity, normality, homoscedasticity, and statistical independence, were assessed. Multicollinearity was assessed using the variance inflation factor (VIF) cutoff of less than 2. All *p-values* are two-tailed and considered statistically significant at $p<.05$, unless noted otherwise.

Sensitivity Analyses

Preliminary analysis showed that a significant number of this sample had a history of homelessness in the past 12 months (n=17). Homelessness may place individuals at a more heightened risk for vulnerability in the contexts of psychosocial and physical well-being and may confound the results. Therefore, sensitivity analyses were conducted only with those participants without a history of homelessness (n=129). In addition, a propensity score analysis using inverse

probability of treatment weighting approach (Austin, 2011) was performed to control for potential effects of past homelessness on loneliness. Propensity score analysis is a technique used to mimic a randomized controlled trial where the characteristics between treatment and control groups are randomly and evenly distributed (Austin, 2011). This method matches individuals who may share similar observable characteristics but may be in different treatment groups. It uses the probability of person receiving the treatment and uses these predicted probabilities or propensities to match the random attribution to either groups. Although past homelessness is not a "treatment" *per se*, propensity score analysis can use any exposure to be modeled as treatment. Propensity score for past homelessness were calculated using a multivariable logistic regression model to account for a variety of statistically significant correlates (history of arrest in the past 12 months, employment status, depressive symptoms, HIV-related stigma, social network size) of homelessness in the current patient characteristics at the bivariate level. Specific propensity scores were computed as the following: for each homelessness observation, the score was calculated by dividing one by the propensity for past homelessness; for no past homelessness observation, the score was calculated by dividing one by one minus the propensity for past homelessness (Austin, 2011). In the regression analysis of loneliness as the outcome, observations were weighted according to the propensity score so that all participants had the same overall propensity to be assigned as having a history of homelessness in the previous 12 months.

Results

A total of 146 older PLWH completed the study. The sample characteristics are presented in **Table 3.1**. The mean age was 56.53 years (SD=4.55), with a range of 22 years. Participants had been living with HIV for an average of 18.10 years (SD=8.36). The study sample was

predominantly African American (AA; 85.6%), male gender (60.3%), heterosexual (63%), and had completed a high school education/GED or greater (78%). Almost 12% of participants (n=17) reported a history of homelessness in the previous 12 months. Of those 17 participants with a history of homelessness, five were female and 16 self-identified as AA. About 25% of participants had a score of 16 or higher on the depression scale, indicating possible clinical depression. The mean T-score for loneliness (PROMIS-SI scale) was 47.19 (10.09) and more than 41% of participants (n=61) were categorized as lonely (T score of 50 or greater).

Bivariate Analysis

Bivariate and multivariable analyses were conducted using the mean T-score for loneliness as the outcome variable. Depressive symptoms (r=.50, p<.001), HIV-related stigma (r=.46, p<.001), social network size (r= -.27, p=.001), HIV-disclosure status (r= -.18, p=.031), comorbidity burden (r=.27, p=.001), and functional status (r=-.21, p=.013) had statistically significant correlations with loneliness.

There were no statistically significant associations between demographic factors (age, gender, years of HIV diagnosis, race/ethnicity, sexual orientation, and levels of education) and loneliness, except for the history of homelessness in the previous 12 months (r=.23, p=.006); therefore, only the history of homelessness was included as a demographic factor in the regression analyses. Marital status was excluded from the analysis because the social network size scale (SNI) assessed marital status.

Multivariable Regression Analysis

The two-step hierarchical multiple regression examining the correlates of loneliness is presented in **Table 3.2**. In the first step, homelessness, comorbidity burden, and functional status

were included. The second step considered study variables including HIV-related stigma, HIV-disclosure status, depressive symptoms, and social network size.

The results of the first step showed that homelessness (β = 0.21, *p*=.007), comorbidity burden (β = 0.24, *p*=.002), and functional status (β = -0.18, *p*=.026) were significant correlates of loneliness and the model explained 15% of the variance in loneliness (R^2 = 0.15, F(3, 142)= 8.35, $p < .001$). In the second step, the addition of study variables in the regression analysis accounted for an additional 26% of the variance in loneliness, with the final model accounting for 41% of the variance in loneliness (R^2 = 0.41, F(7, 138)= 13.76, $p < .001$). Depressive symptoms (β = 0.35, $p < .001$) and HIV-related stigma (β = 0.29, $p < .001$) were significantly associated with loneliness in the final model. Inclusion of the study variables reduced the independent effects of homelessness, functional status, and comorbidity burden on loneliness, rendering their coefficients non-significant.

Sensitivity Analyses

Sensitivity analyses were conducted using the subsample without history of homelessness in the past 12 months (n=129). Results of the subsample were similar to the original results (data not shown). Additionally, the propensity-weighted data results remained similar to that of the original results (data not shown). These similar results from sensitivity analyses provide further credibility and robustness of our original findings.

Discussion

This study investigated correlates of loneliness in older individuals (age ≥50) living with HIV/AIDS. We found that a meaningful proportion of our sample of older PLWH experience loneliness. Higher loneliness was associated with greater HIV-related stigma and depressive

symptoms above and beyond the influence of non-modifiable factors including demographic factors, comorbidity burden, and functional status.

Higher than average levels of loneliness were reported among our sample. The loneliness scale used in this study (PROMIS, 2015) was developed so that the score of 50 is the average score for a representative sample of the United States general population (Cella et al., 2010). Approximately 41% of our participants scored 50 or greater on this instrument, suggesting that this proportion of our sample had higher than the average score (Cella et al., 2010). This is not a surprising finding given the significant prevalence rates of depression among older PLWH (Havlik, Brennan, & Karpiak, 2011) and the relationship between depression and loneliness (Grov et al., 2010). Our finding is similar to a recent study that found a significant proportion of their sample of older PLWH reporting loneliness (Greene et al., 2018) and studies that showed as many as 40% samples containing uninfected older adults reporting feelings of loneliness (Theeke, 2009; Golden et al., 2009; Routasalo, Savikko, Tilvis, Strandberg, & Pitkala, 2006; Savikko, Routasalo, Tilvis, Strandberg, & Pitkala, 2005; Wilson & Moulton, 2010).

Our study found that past history of homelessness and greater disease severity, as indicated by comorbidity burden and functional status, were associated with loneliness. The addition of HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size explained much more of the variance in loneliness. The association between loneliness and disease severity is well-established in the general gerontology literature (Pinquart & Sorensen, 2001). Our study found no significant demographic characteristics related to loneliness except for the past history of homelessness in the previous 12 months prior to the study assessment. Research shows that homeless individuals have small and fragile social networks (Bower, Conroy, & Perz, 2018; Gray, Shaffer, Nelson, & Shaffer, 2016). Homelessness may

disproportionately expose HIV-infected older individuals to additional stressors that predispose them to marginalization and psychosocial vulnerabilities including trauma, financial insecurities, social exclusion, and discrimination (Gray, Shaffer, Nelson, & Shaffer, 2016), which all may further exacerbate loneliness. Although there are no quantitative studies examining loneliness among older HIV samples with past or current homelessness, some research with uninfected adults supports that homelessness is associated with feelings of discrimination and neglect, promoting feelings of isolation (Johnstone, Jetten, Dingle, Parsell, & Walter, 2015). Furthermore, it is recognized that experiences of homelessness exacerbate psychiatric conditions, including schizophrenia and depression (Castellow, Kloos, & Townley, 2015). These conditions have been shown to be associated with loneliness (Badcock et al., 2015). It might be of interest to examine the differences in levels of loneliness in homeless older PLWH based on other inequalities (i.e., due to sexuality, disability, ethnicity, or gender) and mental health conditions that may serve as additional stressors and influence a person's social network.

This study did not support demographic correlates (age, gender, and race/ethnicity) of loneliness shown in numerous studies with uninfected older adults (Hawkley et al., 2008; Cohen-Mansfield & Parpura-Gill, 2007; Theeke, 2009). This might be due to the fact that our sample is considerably younger compared to the studies of loneliness in the uninfected older adults. While "elderly" is defined as aged 60 years or older in the general population, aged 50 years or older is considered "elderly" or "advanced age" in PLWH (Blanco et al., 2012). Considering that growing old with HIV or newly acquired HIV infection at old age are both newly emerging and novel phenomena due to the recent significant advances in cART, findings that have been identified in the general older adult population may not be comparable to this new group of "older" adults.

Depressive symptoms and HIV-related stigma explained most of the variance in loneliness in our sample. This is consistent with the literature that depression is related to loneliness but is a distinct concept (Musich, Wang, Hawkins, & Yeh, 2015). In fact, a mixed methods study describing the experience of depression among uninfected older adults showed that many older persons reported loneliness as a unique proximal factor that precedes depression (Bower et al., 2018). Similarly, using cross-lag path analyses, Cacioppo, Hawkley, and Thisted (2010) found that loneliness predicted changes in depressive symptoms but not vice versa in middle aged and older adults. HIV-related stigma has also been shown to be related to loneliness in other studies (Grov et al., 2010).

Although disclosure of HIV-status and larger social network size were negatively related to loneliness in bivariate levels, these factors were no longer significant when other study variables were introduced. HIV-disclosure status was assessed with only one question as there are no validated or gold standard questionnaires available. It might be of interest for future studies to consider assessing whether there are differences in loneliness depending on individual's disclosure of HIV status to certain groups of contacts (e.g., partner, family members, and/or friends). Despite studies with general older adults suggesting the association between objective indicators of social isolation (i.e., social network size), and loneliness, our study did not support this relationship. This may imply that HIV-related stigma and depressive symptoms are so strongly associated with loneliness that they suppress the effects of social network size on loneliness.

Limitations

This study should be considered with its limitations. The cross-sectional design of the study precludes inferences about causality. Generalizability may also be limited since our sample was predominately male, AA race/ethnicity, heterosexual, and had been living with HIV for many years. However, some of these characteristics are similar to the current HIV epidemic in the South, which indicates predominant rates of HIV infection in males and AAs (CDC, 2017). Although our sample consisted of individuals self-reporting themselves as primarily heterosexuals, which is unlike that of the current HIV prevalence estimates in the United States, our sample reflects the clinic's patient population characteristics. As such, our findings may not be generalizable to those who are not heterosexuals. Temporal effects of loneliness were not assessed and therefore future studies should utilize longitudinal designs to assess for changes and causal relations in loneliness and its related factors. The current study data were collected from a convenience sample of older PLWH attending a comprehensive HIV care clinic in a high resource setting. The recruiting clinic incorporates a "one-stop shop" type of practice and provides multidisciplinary services including psychiatric (group therapy and individual sessions), pharmacy, dental, and primary medical care services. The clinic not only provides medical support but also allows patients to engage in social activities. In fact, many of our study participants were part of support groups from the clinic. Therefore, this may have affected their social network size and its influence on loneliness, and limit generalizability. This setting and sample may not be a representative sample of the general HIV population, and may suggest the possibility of even worse loneliness in resource limiting settings. Accordingly, many factors in the current study may not be applicable to the general HIV population or those who are much more vulnerable such as those who are socially disenfranchised or lack access to care/resources such as persons living in rural areas. Despite these limitations, this study contributes to the

literature by explaining contributing factors to loneliness in older PLWH, which may allow for targeting or adapting interventions more appropriately in reducing loneliness and preventing its negative effects on health outcomes.

Conclusions

A deeper understanding of the correlates of loneliness among this population is needed to address challenges related to health outcomes and improve overall well-being among older PLWH. The current study assessed contributing factors to loneliness in a sample of older PLWH. The results suggest that a meaningful proportion of our sample of older PLWH experience loneliness, and that depression and HIV-related stigma explain a significant amount of loneliness in our sample of older PLWH. These findings therefore imply that targeting HIV-related stigma and depressive symptoms may reduce loneliness in older PLWH. Greater understanding of the mechanisms by which loneliness affects health among older PLWH could help better inform efforts to improve well-being among this patient population.

Table 3.1. Demographic and Clinical Characteristics (N=146)

Characteristic	*n*	%
Race/ethnicity		
African American/Black	125	85.6
White/Non-Hispanic	12	8.2
Other	9	6.2
Gender		
Born Male/Identify Male	88	60.3
Born Female/Identify Female	55	37.7
Born Male/Identify Female	2	1.4
I choose not to answer	1	0.7
Marital status		
Never married/Single	86	58.9
Divorced/Separated	30	20.5
Married/Living with Significant Other	14	9.6
Widow/Widower	14	9.6
Other	2	1.4
Sexual orientation		
Homosexual, Gay, or Lesbian	30	20.5
Heterosexual or Straight	92	63.0
A Man Who Has Sex With Men	6	4.1
Bisexual	16	11.0
Other	2	1.4

History of homelessness in the past 12 month		
No	129	88.4
Yes	17	11.6
Education		
Some high school or less	32	22.0
High school graduate or equivalent (GED)	54	37.0
Some college or higher	60	41.0
HIV disclosure status		
Disclosure to someone	129	88.4
Disclosure to no one	17	11.6
Baseline HIV RNA viral load[a]		
Undetectable (<40 copies/mL)	96	66.2
Detectable	49	33.8
Baseline CD4 T Cell count[c]		
≥ 200 cells/mm^3	130	90.3
< 200 cells/mm^3	14	9.7
Lonely participants[*]	58	39.7

	Mean ± *SD*	**Min**	**Max**
Age	56.53 ± 4.55	50	72
Years since HIV diagnosis	18.10 ± 8.36	2	34
Comorbidity burden	1.28 ± 1.54	0	8
Functional status	7.66 ± 0.78	3	8
HIV-related stigma	1.94 ±1.95	0	6

Depressive symptoms	10.86 ± 10.31	0	47
Social network size	16.14 ± 10.56	0	48
Loneliness	47.19 ± 10.09	33.9	71.8
Baseline Viral Load (copies/mL)[a]	1,178.37 ± 8,799.47	<40[b]	80,030
Baseline CD4+ T Cell Count (cells/mm^3)[c]	539.53 ± 299.88	23	1,789

Notes. *Standardized T-score greater than 50 on PROMIS-Social Isolation scale; a., n=145; b., undetectable viral load; c., n=144; SD=standard deviation

Table 3.2. Multivariable Linear Regression Analysis on Loneliness (N=146)

Variable	*B*	SE *B*	*β*	*p*	R^2	*F*	*Sig*
Step 1					0.15	8.35	**<.001**
History of homelessness	6.65	2.43	0.21	**.01**			
Comorbidity burden	1.57	0.51	0.24	**.00**			
Functional status	-2.26	1.006	-0.18	**.03**			
Step 2					0.41	13.76	**<.001**
History of homelessness	1.27	2.20	0.04	.56			
Comorbidity burden	0.85	0.45	0.13	.06			
Functional status	-1.59	0.86	-0.12	.07			
Depressive symptoms	0.34	0.07	0.35	**<.001**			
HIV-related stigma	1.51	0.38	0.29	**<.001**			
Social network size	-0.10	0.07	-0.10	.14			
Disclosure of HIV status to someone	-1.04	2.21	-0.03	.64			

Notes. SE=Standard Error; Step 1 *adjusted* R^2 =0.13; Step 2 *adjusted* R^2 =0.38.

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CHAPTER 4

SOCIAL ISOLATION AND RETENTION IN CARE IN OLDER PERSONS LIVING WITH HIV/AIDS

Abstract

Introduction: Retention in care (RIC) is important for older persons living with HIV/AIDS (PLWH) to effectively manage not only HIV infection but also age-associated multimorbidities. Evidence is limited on specific factors related to suboptimal RIC only among older PLWH. Guided by Hawkley and Cacioppo's modified Theoretical Model of Loneliness, this study used path analysis to test whether social isolation (social network size and loneliness) affected RIC either directly or indirectly through emotion dysregulation in older PLWH.

Methods: Older PLWH (age 50 years or older) enrolled in an HIV outpatient clinic in the Southeastern region of the United States were followed for a period of 12 months to assess RIC (i.e., adherence to scheduled appointments with their HIV care providers). Social isolation and factors that have been shown to affect RIC were assessed at baseline. Emergent healthcare service use and HIV biomarkers were abstracted from electronic medical records.

Results: Participants included 144 older PLWH with a mean age of 56.5 years. Most participants were male (60.3%), African American/Black (85.6%), and single (59%). There were no direct or indirect effects of social isolation on RIC. RIC was related to sociodemographic factors, risky behaviors, and clinical factors, including past homelessness, monthly income, substance abuse, hospitalization, viral load, and CD4+ T cell count.

Conclusions: Findings suggest that socioeconomic and behavioral vulnerabilities such as homelessness, low income, and substance use are closely tied to RIC among older PLWH. More research is needed to elucidate the pathways by which RIC is affected and to disentangle individual, interpersonal, and organizational/structural factors on RIC in this ever-growing subpopulation of PLWH.

SOCIAL ISOLATION AND RETENTION IN CARE IN OLDER PERSONS LIVING WITH HIV/AIDS

Introduction

The National HIV/AIDS Strategy aims to increase the percentage of persons living with HIV/AIDS who are retained in HIV care from 50.9% in 2010 to 90% by 2020 (Office of National AIDS Policy [NHAS], 2015). Although research suggests that older age is associated with better retention in HIV care (RIC) compared to younger age (Fleishman, Yehia, Moore, Korthuis, & Gebo, 2012), limited evidence on specific factors related to suboptimal RIC among older persons living with HIV/AIDS (PLWH) is currently available. Existing literature supports the effects of social isolation on health care utilization behaviors (HCU) in the general population (Broadhead et al., 1989; Penning, 1995), and a growing body of literature notes the link between social support and treatment adherence in PLWH (DiMatteo, 2004; Magrin et al., 2015), including RIC (Bodenlos et al., 2007; Waldrop-Valverde, Guo, Ownby, Rodriguez, & Jones, 2014). Studies consistently show that older PLWH are at risk for social isolation (Emlet, 2006), perceive barriers to adequate social support (Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005), and experience loneliness (Grov et al., 2010; Greene et al., 2018). However, social isolation has been addressed only to a limited degree in the context of older PLWH, and it remains unknown whether and how social isolation affects RIC.

The advent of antiretroviral therapy (ART) has revolutionized HIV-infection management, improved outcomes, and prolonged longevity of HIV-infected patients. However, as PLWH are living longer and aging, their risk of comorbid conditions increases. The successful management of the health of older PLWH requires consistent engagement in medical care that integrates age-associated multimorbidities and now-chronic HIV infection management through lifelong clinic appointments with a healthcare provider. Poor RIC is associated with numerous

health consequences such as development of an AIDS-defining illness, increased odds of mortality, and poorer viral suppression (Giordano et al., 2007; Mugavero et al., 2009; Park et al., 2007; Ulett et al., 2009). In addition, the number of missed clinic visits have been found to be a significant predictor of having an AIDS-defining CD4+ T cell count whereas the number of kept clinic visits and regular utilization of HIV medical services predicted non-detectable viral load (van den Berg et al., 2005) and lower utilization of acute and emergent health care services (Shapiro et al., 1999). To date, studies have mostly focused on the identification of correlates of RIC in PLWH in general but have not focused primarily on older individuals. Key risk factors to RIC identified include, but are not limited to, demographics, substance use, clinic/healthcare provider factors, clinical (e.g., CD4+ T cell count, viral load, comorbidities) and psychosocial (e.g., HIV-related stigma, depression) factors, and health care utilization (HCU) (e.g., use of emergency department [ED] or acute hospitalization) behaviors (Brandt, Jardin, Sharp, Lemaire & Zvolensky, 2017; Bulsara., Wainberg, & Newton-John, 2018; Giordano et al., 2007; Katz et al., 2013; Mugavero et al., 2009; Park et al., 2007; Rao, et al., 2012; Shapiro et al., 1999; Ulett et al., 2009; van den Berg et al., 2005). However, research is scant on the potential effect of social isolation on RIC and the mechanism of RIC for older PLWH, limiting our understanding of the process by which RIC is affected in this subpopulation of PLWH.

Social isolation is defined as “a state in which the individual lacks a sense of belonging socially, lacks engagement with others, has a minimal number of social contacts and they are deficient in fulfilling and quality relationships” (Nicholson, 2009, p.1346) and contains objective and subjective aspects. Objective aspects of social isolation reflect a quantifiable state of isolation that can be indicated by having a small social network size or low levels of participation in social activities (Cornwell Waite, 2009a; Cornwell & Waite, 2009b). On the other hand,

loneliness reflects a subjective state of isolation and is defined as the discrepancy between actual and desired social relationships (Perlman and Peplau 1982). Research shows that objectively socially isolated persons (i.e., small social network size) are not necessarily lonely, and lonely persons are not necessarily socially isolated in an objective sense, yet some may be both objectively isolated and lonely (Gierveld, Tilburg and Dykstra, 2006). Because both aspects of isolation may affect health in different ways (Cornwell & Waite, 2009b; Holt-Lunstad, Robles, & Sbarra, 2017), both objective and subjective indicators of social isolation need to be assessed concurrently to adequately understand how they may drive health in PLWH especially, older adults who may be at more risk for isolation. Studies on social isolation in HIV-infected samples generally have focused on objective aspects of isolation and comparatively less has been conducted on subjective isolation, or loneliness. Moreover, existing research in older PLWH has frequently examined either social network size or loneliness separately, limiting the understanding of the extent to which social isolation affects health.

Studies show a consistent association between social support and medication adherence. Two meta-analyses showed that functional support (i.e., emotional/perceived support, informative/instrumental support), rather than structural support (i.e., marital status, living arrangement, network size) was more strongly associated with medication adherence in patients with chronic conditions (DiMatteo, 2004; Magrin et al., 2015). On the other hand, a study by Bodenlos and colleagues found that structural support (i.e., number of support network), rather than functional support (i.e., perceived satisfaction with support), was related to appointment adherence in a sample of PLWH (Bodenlos et al., 2007). Similarly, Waldrop-Valverde and colleagues found that use of social support moderated the effect of neurocognitive impairment on appointment adherence among PLWH; those with impaired neurocognitive function and higher

use of support were less likely to miss HIV clinic appointments (Waldrop-Valverde, Guo, Ownby, Rodriguez, & Jones, 2014). This study also showed main effects of social support on higher appointment adherence demonstrating the importance of examining whether PLWH possess adequate social network size and support systems. However, recent studies suggest that older PLWH are socially isolated (Emlet, 2006), tend to live alone and have limited and inadequate social networks compared to their younger counterparts (Schrimshaw & Siegel, 2003; Shippy & Karpiak, 2005), and report negative mood stemming from loneliness (Grov et al., 2010; Greene et al., 2018).

The extent to which social network size and loneliness affects RIC among older PLWH is unknown. Studies with the uninfected adults suggest that social network size and loneliness affect health behaviors, including alcohol abuse, physical inactivity, and smoking (Shiovitz-Ezra & Litwin, 2012; Kobayashi & Steptoe, 2018). Existing studies on the effects of social isolation on HCU behaviors among uninfected individuals with other chronic conditions focus on emergent HCU, including acute hospitalization and ED use, and primary care service use. A study conducted in Sweden found that, although there were no statistically significant differences, older individuals who had more frequent contact with their primary care providers tended to be lonelier and to have lower social network size compared to those who did not have frequent attendance at their primary care clinics (Jakobsson, Kristensson, Hallberg, & Midlöv, 2011). Similarly, a study conducted using the Health and Retirement Study data of community-dwelling older Americans found that loneliness was significantly associated with more primary care provider visits, but not with acute hospitalizations (Gerst-Emerson & Jayawardhana, 2015). In contrast, a study of frequent primary care service users of older adults aged 70 years or older in Canada found that after accounting for covariates, low support networks and loneliness were

not associated with the number of primary care visits (Hand, et al., 2014). It is important to note that a visit to a primary care clinician can be urgent or planned, but it is not always clear whether the primary care visits operationalized and assessed in these studies contain constellations of planned and intentional appointments, or also include urgent or walk-in types of appointments. Blurred distinctions between planned versus unplanned/urgent attendance at primary clinics make it difficult to interpret this set of findings in relation to RIC in older PLWH, where RIC is conceptualized as more intentional self-management behavior, whereas urgent and unplanned clinic visits cannot, necessarily, be conceptualized in this way. With this distinction in mind, a study conducted in Ireland with a sample of older adults (≥65 years of age) found that greater loneliness was independently associated with greater number of ED visits in the previous 12 months but not with *planned* inpatient admissions (Molloy, McGee, O'Neill, & Conroy, 2010). However, this study is limited by its retrospective self-report over the previous year's healthcare service use, the use of a single-item to assess for loneliness, and the lack of a clear definition on *planned* inpatient admissions and how this may have influenced participants' self-report.

In addition to these findings on loneliness and emergent HCU, a systematic review of older adults' social relationships and HCU found that objective isolation was associated with increased rates of hospital readmission and longer hospital stays (Valtorta, Moore, Barron, Stow, & Hanratty, 2018). This review did not find a significant association between objective isolation and primary care service use. However, again, it is not clear whether primary care service use termed in this review was an urgent or planned service. Based on these findings, we aimed to evaluate how both indicators of social isolation may affect RIC, a health-promoting self-management behavior required for older PLWH to optimally manage their health.

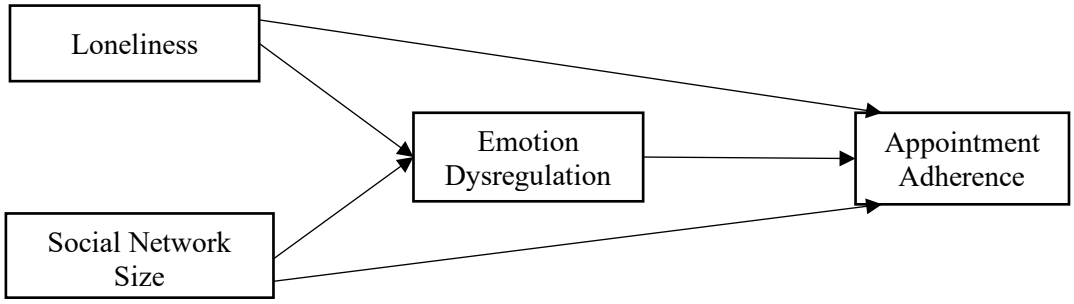
One variable that may help to explain RIC among older PLWH is emotion dysregulation,

defined as difficulties in self-regulation of affective states and in self-control over affect-driven behaviors (Mennin, Heimberg, Turk, & Fresco, 2005). Emotion dysregulation has been shown to be associated with negative affective states, including anxiety and depression, in studies with PLWH (Brandt, Zvolensky, & Bonn-Miller, 2013). Evidence shows that lonely individuals exhibit higher levels of negative affect and lower levels of positive affect than individuals who are not lonely (Hawkley, Preacher, & Cacioppo, 2007) and similar associations, especially with depression, are shown with small social network size (Cho, Olmstead, Choi, Carrillo, Seeman, & Irwin, 2018). Additionally, a recent study showed a moderating effect of emotion dysregulation on the association between depression and HIV medication adherence (Brandt, Bakhshaie, Zvolensky, Grover, & Gonzalez, 2015), such that the effect of depression on medication non-adherence depended on the higher level of emotion dysregulation. Just as depression is associated with medication adherence, we hypothesize that emotion dysregulation may be associated with RIC in older PLWH.

The purpose of this study was to explore the predictive relationships of specific mechanistic pathways of RIC using a modified Theoretical Model of Loneliness (Hawkley & Cacioppo, 2010), which includes social network size, loneliness, and emotion dysregulation to RIC in older PLWH. Hawkley and Cacioppo (2010) suggest that loneliness makes lonely people feel unsafe in their social environment and these feelings perpetuate them to become overly vigilant for social threats, thereby diminishing their capacity to self-regulate emotions and health behaviors (Cacioppo & Hawkley, 2009; Hawkley & Cacioppo, 2010). In other words, when the feelings of loneliness become chronic and persistent sources of distress, the ability to regulate emotion becomes reduced, leading to dysfunctional health behaviors, subsequently affecting health outcomes. Although the effects of social isolation on emotion dysregulation have not been

examined to date, to the extent that lower social network size and higher loneliness are associated with negative affective states, it is postulated that they would be associated with emotion dysregulation. In turn, emotion dysregulation may contribute to a reduced motivation to engage in health behaviors, such as RIC. The Theoretical Model of Loneliness postulates that loneliness potentially influences health via emotional and behavioral self-regulation (Hawkley & Cacioppo, 2010), of which it suggests a direct path from loneliness to emotion dysregulation and health behavior, and an indirect path from loneliness to health behavior via emotion dysregulation. In this study, the Model of Loneliness provided an *a priori* model and social network size was added along with loneliness to assess both objective and subjective aspects of isolation simultaneously. **Figure 4.1** presents a set of hypotheses about the relationships between study variables using the modified Model of Loneliness.

Figure 4.1. Hypothesized *a priori* Model of Social Isolation and Retention in Care



In line with the Model of Loneliness, we hypothesized that both indicators of social isolation will have direct effects on RIC and also indirect effects through emotion dysregulation among our sample of older PLWH. We also explored the differences in participant characteristics depending on their level of RIC to observe whether there are certain patient characteristics that

could help identify and target those older patients at risk for suboptimal RIC.

Methods

Study Design

This study incorporated a cross-sectional in-person baseline visit followed by prospective data collection on outpatient HIV clinical provider visits from electronic medical records (EMR) for 12-months post-baseline visit. Emory University's Institutional Review Board (IRB) and the recruiting hospital and clinic's research oversight committee before start of the study.

Participants & Setting

English-speaking older PLWH were recruited through flyers, word of mouth, and healthcare provider referrals. Eligible individuals were 50 years or older and HIV infected, able to speak and understand English, and had at least one medical visit established in the recruiting clinic. The recruiting clinic provides primary HIV-related and non-HIV related medical services to over 5,800 PLWH in Atlanta, GA, and draws uninsured, underinsured, and economically disenfranchised patients from the large, urban Atlanta area and surrounding communities. Patients at the recruiting clinic were routinely scheduled for a minimum of one HIV medical provider visit every 6 months.

Exclusion criteria were severe learning disabilities, intellectual disabilities, psychotic disorders, and severe cognitive impairment/dementia that inhibits an individual's ability to consent to the study and complete study assessments. After prescreening and provision of informed consent, eligibility criteria were confirmed by EMR (Epic Systems Corporation, Veronia, WI). Due to the likelihood of low literacy, a consent post-test was given to assess the

capacity to provide informed consent prior to enrollment. Individuals who failed the consent post-test within three attempts were excluded (n=3).

Data Collection

After obtaining informed consent and HIPAA authorization, participants completed a baseline assessment that included a battery of questionnaires on study variables and demographics via Research Electronic Data Capture (REDCap) on a computer in a private research office. REDCap is a secure, web-based, electronic data capture tool allowing online survey entry (Harris et al., 2009) in compliance with the University's HIPAA policies and procedures. Baseline data were collected between August 2016 and April 2017. Participants were compensated with $25 in cash upon completion of baseline questionnaires.

Over the 12-months after completion of the baseline visit, information on the dates and the status of outpatient HIV clinical provider visits were abstracted from patient EMR from August 2017 to April 2018. Consistent with other studies and definitions, HIV clinical visits were defined as visits made to a HIV care provider including the MD, DO, PA, and NP in the ambulatory setting. Specialty care visits (e.g., mental health, cardiology, diabetes, etc.), annual well-visits including gynecologic visits, walk-in visits, nurse visits (e.g., B12 injection, wound management, etc.), and phlebotomy visits were excluded. Approximately 10% of all data were randomly re-abstracted by the lead author to ensure the data quality and to minimize discrepancies and errors. Of the total 146 participants enrolled in the study, two participants had no visits scheduled since the baseline assessment date, and thus were removed from the analysis.

Measures

Endogenous/Outcome Variables

Retention in care was operationalized as *appointment adherence*, which was computed by calculating the number of attended HIV care visits in the numerator and the number of total scheduled visits ("attended" plus "missed" visits) in the denominator during the 12-month prospective observation period (Mugavero, Davila, Nevin, & Giordano, 2010). The computed score was multiplied by 100 to represent a proportion of attended scheduled appointments (range=0-100%). HIV care visits status were coded as "attended," "no-show," or "canceled." A visit was considered missed if the status was "no-show" and not missed if the status was "attended." A visit that was cancelled either by the provider or the patient was excluded from the calculation.

Emotion dysregulation was measured using Gratz and Roemer's Difficulties in Emotion Regulation Scale (DERS; Gratz & Roemer, 2004), which was developed to assess multiple aspects of emotion dysregulation and includes 36-items rated on a 5-point Likert scale (1=*almost never* to 5=*almost always*). Higher scores suggest greater problems with emotion regulation. DERS has high internal consistency (Cronbach's α from .80 to .89), test–retest reliability (r = .88), and adequate construct and predictive validity among adolescents, young adults, and community dwelling older adults (Staples & Mohlman, 2012). The DERS has been used in previous studies with the HIV/AIDS population (Brandt, Jardin, Sharp, Lemaire, & Zvolensky, 2017; Leyro, Vujanovic, & Bonn-Miller, 2015). The current study had excellent internal consistency (α= 0.93).

Exogenous/Independent Variables

Social network size was measured using the Social Network Index (SNI), which assesses

social contact with or participation in 12 types of social relationships or social activities at least once every 2 weeks in person or on the phone (Bickart, Wright, Dautoff, Dickerson, & Barrett, 2011; Cohen, Doyle, Skoner, Rabin, & Gwaltney, 1997). The types of social relationships or activities include relationships with a spouse, parents, parents-in-law, children, other close family members, close neighbors, friends, colleagues/coworkers, schoolmates, fellow volunteers, members of groups without religious affiliation, and members of religious groups (Cohen et al., 1997). The total number of people with whom the participants have regular contact was summed across the 12 possible social relationships, reflecting the *overall social network size*. A higher score indicates more social connectedness and lower score indicates more social isolation. SNI was utilized on a sample of older adults in a number of studies (Bickart et al., 2011; Cohen et al., 1997).

Loneliness was measured using the Short Form 8a of the Patient-Reported Outcomes Measurement Information System (PROMIS)-Social Isolation (SI) item bank. The PROMIS measures are standardized based on common metrics that allow for comparisons across domains, across chronic diseases, and with the general population (Cella et al., 2010). The PROMIS-SI scale is centered on the mean of a calibration sample with generally more chronic illnesses than the general population in the United States (PROMIS, 2015). The PROMIS-SI instrument uses 8-items to assess *perceptions* of being avoided, excluded, detached, disconnected from, or unknown by others on a 5-point Likert scale (1=Never to 5= Always; PROMIS, 2015). Items were scored by summing the response values to each question to create a total raw score. Each total raw score was then converted to a T-score metric with a mean of 50 and a standard deviation (SD) of 10 (Cella et al., 2010), following the score conversion table in the scoring instruction (PROMIS, 2015). A higher T-score indicates greater loneliness and T-score of 50

represents an average score of loneliness in average Americans. The Cronbach's alpha for our sample was 0.95.

Covariates. Variables selected for assessment were based on previous literature that had shown significant associations with RIC.

Psychosocial, behavioral, and provider factors, including depression, HIV-related stigma, substance use, and attitude towards healthcare provider, are consistently associated with medication adherence (Brandt, Jardin, Sharp, Lemaire& Zvolensky, 2017; Katz et al., 2013; Rao, et al., 2012) and RIC (Bulsara., Wainberg, & Newton-John, 2018), thus these variables were also considered for their association with RIC. **Depressive symptoms** were assessed using the Center for Epidemiologic Studies Depression Scale Revised (CESD-R; Eaton, Smith, Ybarra, Muntaner, & Tien, 2004). The CESD-R contains 20 items that assess nine symptoms of depression (dysphoria, anhedonia, appetite, sleep, concentration, worthlessness, fatigue, agitation, and suicidal ideation) in accordance with the Diagnostic and Statistical Manual (DSM-V) diagnostic criteria for Major Depressive Disorder. Participants answer 0= "Not at all or less than one day" to 3= "Nearly every day for 2 weeks," with possible scores ranging from 0 to 60. A score ≥16 indicates at risk for clinical depression. In this sample, the internal consistency reliability was good (Cronbach's α= 0.93). **HIV-related stigma** was measured with Kalichman et al.'s Internalized AIDS-Related Stigma Scale (Kalichman et al., 2009), which contains 6 items rated dichotomously (1=agree, 0=disagree), with scores ranging from 0 to 6. A higher score is indicative of greater HIV-related stigma. The internal consistency reliability (Cronbach's α= 0.83) was good in this sample. **Substance use** including drug and alcohol use were collected using the 10-item Drug Abuse Screening Test (DAST-10; Skinner, 1982) and Alcohol Use

Disorders Identification Test (AUDIT-10) (Reinert & Allen, 2007) scales. DAST-10 and AUDIT-10 assesses perceptions of problematic substance and alcohol use during the previous twelve months, respectively. DAST-10 responses are rated dichotomously (1=yes, 0=no), with scores ranging from 0 to 10. Scores 0-2 indicate no to low level of problems related to drug abuse and scores 3-10 indicate moderate to severe levels of drug abuse problems. The scale demonstrated good reliability in our sample (Cronbach's $\alpha = .80$). AUDIT-10 responses are scored on a 3-point and 5-point Likert scale and total scores range from 0–40, with a higher score reflecting more problematic drinking. A score of eight or greater indicates being at-risk for harmful drinking. The scale demonstrated adequate reliability (Cronbach's $\alpha = .71$) in our sample. **Provider factors** were assessed by using the 19-item Attitudes toward HIV Healthcare Providers Scale (Bodenlos et al., 2007). This scale examines one's attitude toward their HIV care team. Items are rated on a 6-point Liker scale (strongly agree to strongly disagree). Scores are summed with higher scores indicating a more positive attitude and satisfaction. In this sample, internal consistency reliability was good (Cronbach's $\alpha= 0.96$).

Disease status and emergent health care utilization behaviors, including lab values (HIV viral load, CD4+ T cell count), emergency department (ED) visits, and hospitalizations have been associated with RIC (Giordano et al., 2007; Mugavero et al., 2009; Park et al., 2007; Shapiro et al., 1999; Ulett et al., 2009; van den Berg et al., 2005) and were obtained from EMR. The **lab values** reported within the closest time from baseline study visit were selected, not to exceed two months (i.e., the lab reports selected were ±2 months from the baseline visit). Undetectable viral load (i.e., viral suppression) was reported as EMR lab value less than 40 copies/mL. **ED visits** were categorized as having any ED visits during the 12-month prospective data collection period or not, and **hospitalizations** were categorized as having any hospitalizations during the 12-

month prospective data collection period or not. **Comorbidity burden** was captured using the self-reported version of the Charlson Comorbidity Index (CCI; Charlson, Pompei, Ales, & MacKenzie, 1987). The CCI includes 19 conditions in which participants were asked to identify ("Yes" or "No") the conditions that they were diagnosed. These conditions included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, connective tissue disease, gastrointestinal disease, mild and serious liver disease, uncomplicated and complicated diabetes mellitus, hemiplegia, moderate and severe renal disease, cancer, leukemia, lymphoma, and secondary metastasis. The comorbidities were assigned a weight based on the adjusted 1-year mortality risk (Charlson et al., 1987). AIDS diagnosis was omitted from the CCI in our study as its weight is outdated in the current era of combination antiretroviral therapy (Zavascki & Fuchs, 2007) and age was not adjusted in this study as our sample consisted only of those who are aged 50 years old or older. The CCI has strong construct validity and reliability (Hall, 2006) and has been used in previous studies with PLWH (Lohse et al., 2011; Rodriguez-Penney et al., 2013).

Sociodemographic characteristics including age, gender, sexual orientation, race/ethnicity, education level, monthly household income, presence/absence of health insurance, and past history of homelessness were collected via self-report. Past history of homelessness was categorized as being homeless in the past 12 months or not. Time required to travel to the clinic and transportation type were self-reported.

Data analysis

Descriptive statistics, bivariate analysis, and logistic regression modeling were performed using SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0.

Armonk, NY: IBM Corp.). Measured variable path analysis was conducted using MPlus statistical software version 8.2 (Muthén and Muthén. Released 2018. MPlus for Windows, version 8.2. Los Angeles, CA: Muthén and Muthén). The significance level was set at 0.05 for all analyses, unless noted otherwise.

Descriptive statistics (counts and percentages for categorical variables and means [*M*] and standard deviations [*SD*] for continuous variables) and measures of central tendency were assessed for all study variables. When the cases of individuals with perfect (100%) appointment adherence (n=77) were excluded, appointment adherence was normally distributed. This distribution implies that there are two underlying populations: those with perfect appointment adherence and those with less than perfect appointment adherence. The goal for RIC is to achieve viral suppression, primarily, and improve CD4+ T cell count. Therefore, cross-tabulation and Chi-square tests on the relationships between different appointment adherence cutoffs and HIV-related clinical outcomes (i.e., viral suppression and non-AIDS-defining CD4+ T cell count) were conducted to determine a meaningful cutoff that reflects outcomes for our sample (**Appendix H**). The results show that the cutoff of 80% and 85% had significant differences in viral suppression ($p<.05$). However, the cutoff of 85% also showed statistically significant difference in CD4+ T cell count ($p<.01$). Since the goals of viral suppression and CD4+ T cell count are complementary, the cutoff of 85% was selected to categorize participants depending on their rate of appointment adherence: suboptimal appointment adherence (≤85%) and optimal appointment adherence (>85%).

To evaluate the differences in participant characteristics by appointment adherence, independent t-tests and Chi-square tests of independence were used as appropriate. To assess which covariates should be included in the path model as control variables, a sequential logistic

regression was used. Covariates that had a statistically significant difference (p<.10) between the two adherence categories were entered in the first block and exogenous variables were added in the second block. The Nagelkerke R^2 value was used to estimate variation in optimal adherence (>85%) explained by the model. The Hosmer and Lemeshow Goodness of Fit Test was used to evaluate the model's fit. Covariates that showed association with appointment adherence in logistic regression with p<.10 were controlled in the subsequent path analysis. Lastly, a theoretically derived proposed path model (**Figure 4.1**) was tested to assess the pathways by which social network size, loneliness, and emotion dysregulation affect appointment adherence using robust weighted least squares estimation method (WLSMV). The WLSMV estimator is robust to deviations from model assumptions, allows modeling with a binary outcome variable, and provides overall fit statistics for model testing (Muthén & Muthén, 1998-2017). To assess the model fit, several indices were used: the χ^2 test (χ^2), the comparative fit index (CFI), the Tucker-Lewis index (TLI), and the Root Mean Squared Error of Approximation (RMSEA) with a 90% confidence interval (CI). Non-significant χ^2, CFI and TLI of greater than 0.95, and the RMSEA of no more than 0.08 indicate a good fit (Hooper, Coughlan, & Mullen, 2008; Kline, 2005).

Results

A total of 146 participants were enrolled in the study. Two participants were excluded due to the absence of main outcome data, which resulted in the final sample of 144. The study sample was predominantly African American (AA) (85.6%), male gender (60.3%), heterosexual (63%), and had completed a high school education/GED or greater (78%). Almost 81% of participants (n=117) self-reported having some type of health care coverage, which included either or both private and public payer coverages. Most participants (n=96) relied on public transportation as

the main method of travelling to their HIV clinic, with 41% of participants reporting 30 minutes to 1-hour travel time. Seventeen reported past homelessness in the previous 12 months at the time of the baseline visit. Of those seventeen participants with a history of homelessness, five were female and sixteen self-identified as AA. Details on study participant characteristics are listed in **Table 4.1**.

Table 4.1. Demographic and Clinical Characteristics (N=146)

Characteristic	***n***	**%**
Race/Ethnicity		
African American/Black	125	85.6
White/Non-Hispanic	12	8.2
Other	9	6.2
Gender		
Born Male/Identify Male	88	60.3
Born Female/Identify Female	55	37.7
Born Male/Identify Female	2	1.4
I choose not to answer	1	0.7
Marital Status		
Never married/Single	86	58.9
Divorced/Separated	30	20.5
Married/Living with Significant Other	14	9.6
Widow/Widower	14	9.6
Other	2	1.4
Sexual Orientation		
Homosexual, Gay, or Lesbian	30	20.5

Heterosexual or Straight	92	63
A Man Who Has Sex with Men	6	4.1
Bisexual	16	11.0
Other	2	1.4
Education		
Some high school or less	32	22.0
High school graduate or equivalent (GED)	54	37.0
Some college or higher	60	41.0
Presence of healthcare coverage	117	80.8
History of homelessness in the past 12 months		
No	129	88.4
Yes	17	11.6
Type of transportation to the clinic		
Public transportation (Bus, disability van, taxi)	96	65.8
Private vehicle (own car, borrowed car)	39	26.7
Rides from family/friends/others	3	2.0
Walking	8	5.5
Time required to travel to the clinic		
Less than 30 minutes	43	29.5
30 minutes to 1 hour	60	41.1
1 hour to 2 hours	37	25.3
2 hours to 3 hours	6	4.1
Baseline HIV RNA viral load [a]		
Undetectable (<40 copies/mL)	96	66.2
Detectable	49	33.8

Any Hospitalization in the 12-month data collection[a]	13		8.9
Any ED visits in the 12-month data collection[a]	26		17.8
	Mean ± SD	**Min**	**Max**
Age	56.53 ± 4.55	50	72
Years since HIV diagnosis	18.10 ± 8.36	2	34
Monthly income	957.63 ± 686.72	0	6,500
Baseline CD4+ T Cell Count (cells/mm^3)[b]	539.53 ± 299.88	23	1,789
Baseline HIV RNA viral load (copies/mL)[a]	1,178.37 ± 8,799.47	<40[c]	80,030
Depressive symptoms	10.86 ± 10.31	0	47
HIV-related stigma	1.94 ± 1.95	0	6
Comorbidity burden	1.28 ± 1.54	0	8
Drug abuse (DAST-10)	1.16 ± 1.87	0	9
Alcohol abuse (AUDIT-10)	2.35 ± 3.56	0	20
Attitudes toward healthcare provider	102.76 ± 13.53	35	114
Emotion dysregulation	71.22 ± 20.11	36	136
Social network size	16.14 ± 10.56	0	48
Loneliness	47.19 ± 10.09	33.9	71.8
Appointment Adherence[b]	81.03 ± 24.16	0	100
Total number of scheduled visits[b,d]	5.02 ± 2.56	1	17
Canceled visits[b]	0.88 ± 1.14	0	6
Missed visits[b]	0.97 ± 1.52	0	9
Attended visits[b]	3.21 ± 1.39	0	10

Notes. a., n=145; b., n=144; c., undetectable viral load; d., including canceled visits; ED=Emergency department; DAST-10=10-item Drug Abuse Screening Test; AUDIT-10=10-item Alcohol Use Disorders Identification Test

During the 12 months prospective EMR data collection, a range of 1 to 17 visits were scheduled, with most participants having between 3 and 7 scheduled visits (*M*=5.02, *SD*=2.56). Appointment adherence ranged from 0% to 100% (*M*=81.17, *SD*=25.93). Seventy seven participants had 100% appointment adherence, indicating that they adhered to all of their scheduled appointments. Appointment adherence was dichotomized into a binary, categorical variable (see **Table 4.2**) based on the findings that this cut-off had statistically difference in both HIV viral load and CD4+ T cell count: "optimal appointment adherence (>85%)" and "suboptimal appointment adherence (≤ 85%)."

Table 4.2. Comparison of Appointment Adherence Cutoffs on HIV Biomarkers (N=144)

a. Appointment adherence cutoff of 75% and HIV viral load (VL)

		Detectable VL[a]	**Undetectable VL[b]**	**Total**	
Appointment Adherence	**0-75%**	25	32	57	($X^2(1)=4.70$,
	76-100%	23	64	87	$p=.030$)
	Total	48	96	144	

b. Appointment adherence cutoff of 80% and HIV VL

		Detectable VL[a]	**Undetectable VL[b]**	**Total**	
Appointment Adherence	**0-80%**	27	33	60	($X^2(1)=6.30$,
	81-100%	21	63	84	$p=.012$)
	Total	48	96	144	

c. Appointment adherence cutoff of 85% and HIV VL

	Detectable VL[a]	**Undetectable VL[b]**	**Total**	

Appointment Adherence	**0-85%**	28	35	63	($X^2(1)=6.22$, $p=.013$)
	86-100%	20	61	81	
	Total	48	96	144	

d. Appointment adherence cutoff of 100%[c] and HIV VL

		Detectable VL[a]	**Undetectable VL[b]**	**Total**	
Appointment Adherence	**<100%**	29	38	67	($X^2(1)=5.58$, $p=.018$)
	100%	19	58	77	
	Total	48	96	144	

e. Appointment adherence cutoff of 80% and CD4+ T cell count

		AIDS-defining CD4+ T cell count[d]	**Non-AIDS-defining CD4+ T cell count[e]**	**Total**	
Appointment Adherence	**0-80%**	10	50	60	($X^2(1)=5.65$, $p=.017$)
	81-100%	4	80	84	
	Total	14	130	144	

e. Appointment adherence cutoff of 85% and CD4+ T cell count

		AIDS-defining CD4+ T cell count[d]	**Non-AIDS-defining CD4+ T cell count[e]**	**Total**	
Appointment Adherence	**0-85%**	11	52	63	($X^2(1)=7.64$, $p=.006$)
	86-100%	3	78	81	
	Total	14	130	144	

Notes. a. HIV viral load ≥40 copies/mL; b., HIV viral load <40 copies/mL; c. same distribution and results

with 90% cutoff; d., CD4+ T cell count <200 cells/mm^3; e., CD4+ T cell count ≥200 cells/mm^3

Of 144 participants, 81 participants had optimal appointment adherence and 63 participants had suboptimal appointment adherence (**Table 4.3**). Significant differences (p <.10) between the two appointment adherence categories were noted in monthly household income (p=.02), past homelessness (p<.001), baseline CD4+ T cell count (p=.006), baseline viral load (p=.01), hospitalization during the 12-month prospective data collection period (p=.05), attitude towards provider (p=.07) and alcohol (p=.08) and drug use (p=.003). For example, participants in the suboptimal appointment adherence category were more likely to have AIDS-defining baseline CD+ T cell count and detectable viral load than those in the optimal appointment adherence category; participants in the suboptimal appointment category scored much higher on drug use (M=1.68, SD=2.33, n=63) than those in the optimal appointment adherence category (M=0.77, SD=1.30), p=.003. No statistically significant differences in gender, sexual orientation, race/ethnicity, education levels, transportation type, and length of travel time to clinic were found (p>.10).

Table 4.3. Differences in Characteristics by Appointment Adherence (N=144).

	Suboptimal Appointment Adherence ≤ 85% (n=63)	**Optimal Appointment Adherence >85% (n=81)**	***p***
	Frequencies		
Gender ($\chi^2(2)=0.71$)			.70
Male	40	46	
Female	22	33	
Other	1	2	
Race/ethnicity ($\chi^2(2)=2.45$)			.29

African American/Black	57	66	
White/Non-Hispanic	3	9	
Other	3	6	
Age ($\chi^2(1)=0.03$)			.86
≥ 60	14	19	
50-59	49	62	
Education ($\chi^2(2)=0.83$)			.66
Some high school or less	15	15	
High school graduate or equivalent (GED)	24	30	
Some college or higher	24	36	
Monthly household income ($\chi^2(1)=5.20$)			**.02**
≤ $1,000	50	50	
> $1,000	13	31	
History of homelessness ($\chi^2(1)=19.87$)			**<.001**
Yes	16	1	
No	47	80	
Baseline CD4 T Cell count ($\chi^2(1)=7.64$)			**.01**
≥ 200 cells/mm^3	52	78	
< 200 cells/mm^3	11	3	
Baseline Viral suppression <40 copies/mL ($\chi^2(1)=6.22$)			**.01**

Yes	35	61	
No	28	20	
Hospitalization in the 12-month observation ($\chi^2(1)=3.77$)			**.05**
Yes	9	4	
No	54	77	
ED use in the 12-month observation ($\chi^2(1)=0.03$)			.87
Yes	11	15	
No	52	66	
	Mean (SD)		
Age	56.64 (4.76)	56.37 (4.44)	.73
Years since HIV diagnosis	19.10 (8.02)	17.25 (8.66)	.19
Social network size	15.30 (10.68)	16.49 (10.44)	.50
Loneliness	47.43 (9.07)	47.27 (10.86)	.93
Emotion dysregulation	70.62 (20.96)	71.89 (19.69)	.71
Depressive symptoms	10.92 (10.12)	11.04 (10.55)	.95
HIV-related stigma	1.95 (1.90)	1.91 (2.00)	.91
Comorbidity burden	1.22 (1.38)	1.33 (1.68)	.67
Attitude towards provider	105.22 (11.97)	101.05 (14.54)	**.07**
Alcohol use (AUDIT-10)	2.97 (4.25)	1.90 (2.87)	**.08**
Drug use (DAST-10)	1.68 (2.33)	0.77 (1.30)	**.00**

Notes. ED=Emergency department; SD=standard deviation; AUDIT-10=10-item Alcohol Use Disorders Identification Test; DAST-10=10-item Drug Abuse Screening Test

Variables that had significant differences ($p<.10$) on two appointment adherence categories were entered sequentially using logistic regression (Model 1). Of 17 participants with past homelessness, all but one were in the suboptimal appointment adherence category. Therefore, due to high collinearity with the outcome (appointment adherence), past homelessness was removed from the analyses. The addition of exogenous variables into the second step (Model 2) did not change the results significantly. Monthly income (B=0.80, p=.07), baseline CD4+ T cell count (B= 1.45, p=.05), and drug use (B=-0.28, p=.02) were significantly related to appointment adherence (**Table 4.4**), thus these variables were retained as covariates in the subsequent path analysis. Participants in higher income category (>$1,000) were twice as likely as those in the lower income category to be optimal appointment adherers. Participants with higher CD4+ T cell count (≥200 cells/mm^3) were 4.3 times more likely to be optimal appointment adherers than those with AIDS-defining CD4+ T cell count. The odds of optimal appointment adherence were reduced by 76% with each additional increase in the score for the drug use scale. This model explained 26% of the variance in optimal appointment adherence (Nagelkerke R^2) and correctly classified 73.6% of optimal appointment adherence (cut off 0.5). The Hosmer and Lemeshow test indicated the model was a good fit (p=.43). Because having past homelessness may affect behaviors and outcomes, a separate regression analysis was conducted using the cases without past homelessness (n=127). The results were similar to the results using the full sample, suggesting robustness of our original results (data not shown).

Table 4.4. Logistic Regressions on Optimal (>85%) Appointment Adherence (N=144)

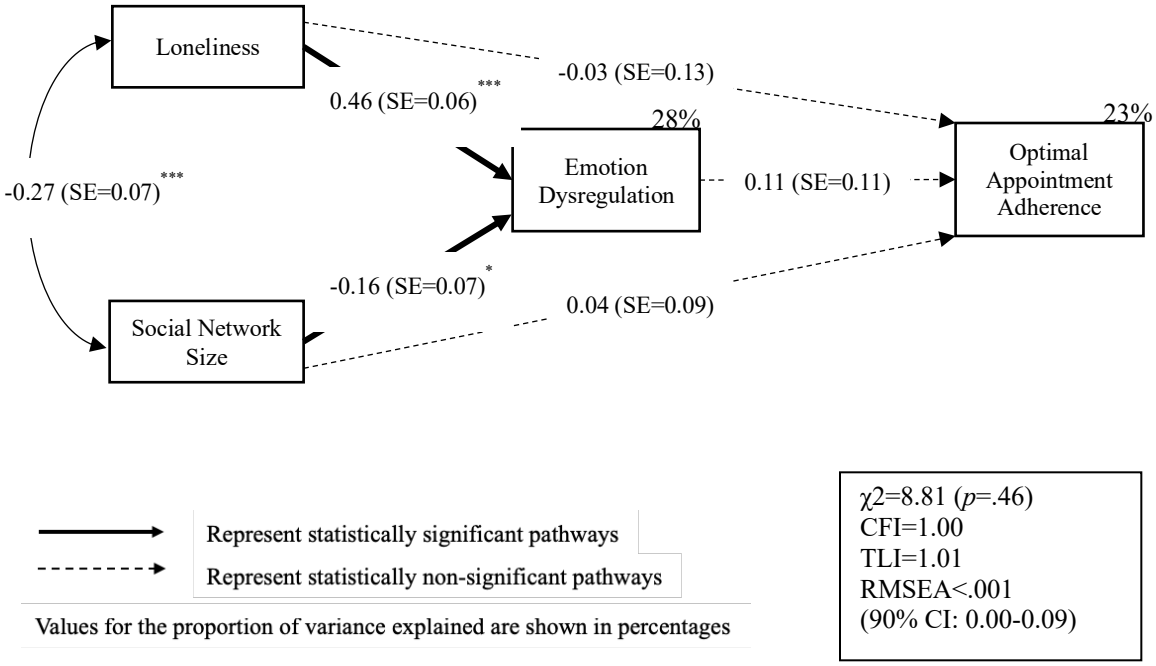
	Model 1			**Model 2**		
Variable	*B*	SE	OR	*B*	SE	OR
Monthly income						

≤ $1,000		*REF*			*REF*	
> $1,000	0.81	0.43	**2.25***	0.80	0.44	**2.23***
Viral load						
Detectable		*REF*			*REF*	
Undetectable	0.64	0.40	1.90	0.64	0.41	1.90
CD4+ T cell count						
<200		*REF*			*REF*	
≥200	1.49	0.73	**4.46****	1.45	0.73	**4.28****
Hospitalization						
Yes		*REF*			*REF*	
No	0.81	0.67	2.26	0.78	0.67	2.17
Alcohol use	-0.03	0.06	0.97	-0.03	0.06	0.97
Drug use	-0.27	0.12	**0.77****	-0.28	0.12	**0.76****
Attitude towards provider	-0.03	0.02	0.97	-0.03	0.02	0.97
Emotion dysregulation				0.01	0.01	1.01
Social network size				0.01	0.02	1.01
Loneliness				-0.01	0.02	1.00
χ^2	29.97, *df*=7, *p*<.001			30.55, *df*=10, *p*<.001		
Nagelkerke R^2	25%			26%		
Hosmer and Lemeshow test	*p*=.42			*p*=.43		
Classification accuracy (% of optimal appointment adherence)	72.2			73.6		

Notes: $^{*}p$ <.10; $^{**}p$ < .05; $^{***}p$ <.001, two-tailed

The proposed path model operationalized adherence as binary (0=suboptimal, 1=optimal appointment adherence). Fit indices reflected very good fit between the model and the sample data: χ^2=8.81 (p=.46), CFI=1.00, TLI=1.01, RMSEA<0.001 (90% CI: 0.00-0.09). The standardized estimates for the individual paths in the model were examined with respect to the hypotheses. As illustrated in **Figure 4.2**, there was a significant direct relationship between loneliness and emotion dysregulation (β=0.46, SE=0.06, p<.001). The direct effect of social network size on emotion dysregulation was also significant (β=-0.16, SE=0.07, p=.01). The interpretation of these standardized coefficients is as follows: every standard deviation increase in loneliness was associated with a 0.46 standardized deviation increase in emotion dysregulation. Loneliness and social network size explained 28% of the variance in emotion dysregulation (R^2=.28).

Figure 4.2. Final path diagram on optimal appointment adherence (N=144)



Notes. SE=standard error. Standardized path coefficients (SE) are reported. Non-significant and significant paths are illustrated by dotted and solid arrows, respectively. The analysis used robust

weighted least-squares estimation method and adjusted for baseline CD4+ T cell count, monthly income, and drug use on optimal (>85%) appointment adherence.

*p<.05, **p <.01***p<.001, two-tailed

However, neither social network size nor loneliness had significant direct effects on optimal appointment adherence, after taking control variables into account: the direct path between loneliness and optimal appointment adherence was non-significant (β=-0.03, SE=0.13, p=.82); the direct path between social network size and optimal appointment adherence was non-significant (β=0.04, SE=0.09, p=.68); and the direct path between emotion dysregulation and optimal appointment adherence was non-significant (β=0.11, SE=0.11, p=.33). As would be expected from these results, the indirect effect was also non-significant.

Discussion

Retention in care (RIC) is an important self-management behavior for effectively managing what is now conceptualized as chronic HIV infection and other chronic conditions that OPLWH may develop with increasing age. Although predictors of RIC are well recognized among HIV-infected patients in general, whether and how social isolation affects RIC is not understood. Further, the characteristics that may predispose older PLWH for poor RIC are not known. This study explored the differences in participant characteristics depending on their level of RIC and examined the mechanistic pathways of social isolation (social network size and loneliness) on RIC either directly or indirectly through emotion dysregulation, using the modified Theoretical Model of Loneliness (Hawkley & Cacioppo, 2010) as a guiding framework. We hypothesized that both subjective and objective social isolation would be associated with appointment adherence and that emotion dysregulation would mediate the

association.

Our results indicated that more than half of our sample was optimally retained in care (>85% adherence to scheduled appointments), whereas the remaining sample was sub-optimally (≤85% adherence to scheduled appointments) retained in care. We explored differences in characteristics between optimal appointment adherers and suboptimal appointment adherers to identify those patients at a greater risk for low RIC. We found that those with lower monthly income, past homelessness, detectable baseline viral load, AIDS-defining baseline CD4+ T cell count, at least one acute hospitalization within 12 months , better attitudes toward their HIV provider, and problematic alcohol and drug use were more likely to have suboptimal appointment adherence. Although studies found that these factors have varying directionality—for example, some studies show that higher CD4+ T cell count to be related to lower RIC (Yehia et al., 2015), yet other studies show that lower CD4+ T cell count to be related to lower RIC (Tedaldi et al., 2014; Wohl et al., 2011)— each of these characteristics has been associated with RIC (Aidala, Lee, Abramson, Messeri, & Siegler, 2007; Bulsara, Wainberg, & Newton-John, 2018; Yehia et al., 2015). It is also important to note that all but one participant with past homelessness was in the suboptimal appointment adherence category in our sample. These characteristics suggest that individuals who are sub-optimally retained in care may face a myriad of socioeconomic and behavioral vulnerabilities that prohibit them from adequately engaging in care. Socioeconomically challenging environments such as unstable housing or homelessness and having no or low income may trigger a cascade of stressors that may serve as underlying risk factors for suboptimal RIC, such as having to make a living to avoid financial obstacles and meeting the basic needs as their first priority (Warren-Jeanpiere, Dillaway, Hamilton, Young, & Goparaju, 2014) instead of attending medical appointments. Although further hypothesis testing

is needed, it makes logical sense that these disadvantaged suboptimal adherers may utilize more emergent and acute inpatient services such as acute hospitalization due to limited engagement in care and inadequate management of their health. More studies are needed to clarify RIC rates among those with current or past homelessness or with unstable housing and those with socioeconomic and structural inequities, and evaluate whether providing housing or telemedicine might allow for better RIC and outcomes.

Our *a priori* path model included social network size, loneliness, emotion dysregulation, and appointment adherence. Emotion dysregulation was not significantly related to appointment adherence in the current study. Our finding is consistent with a cross-sectional retrospective study that assessed the effects of depressive symptoms, one indicator for emotion dysregulation, on appointment adherence (Bodenlos et al., 2007), yet contradicts other research that has shown a significant relationship between depression and other HIV adherence behaviors such as medication adherence (Gonzalez, Batchelder, Psaros, & Safren, 2011). It may be plausible that emotion dysregulation is uniquely related to medication adherence but not with RIC because medication adherence requires more complex self-managing capacity with higher levels of motivation and thinking and problem-solving skills especially when surrounding contextual factors are not ideal (e.g., delaying treatment dose due to being with other people who do not know about one's HIV status). The complexity of ART regimens and daily dosing of ART in addition to administration of multiple medications for other health conditions may also complicate HIV medication adherence behavior. On the other hand, RIC is a planned behavior that individuals can prepare and manage before unfavorable contextual circumstances arise and may require less effort than medication adherence. Therefore, emotion dysregulation may not influence this type of management behavior to the same degree as with other HIV adherence

behaviors.

Despite some evidence of the link between social isolation and health care utilization (HCU) for other chronic conditions among uninfected older adults (Molloy, McGee, O'Neill, & Conroy, 2010; Valtorta, Moore, Barron, Stow, & Hanratty, 2018), our findings show that neither social network size nor loneliness directly or indirectly influence RIC. These results concur with previous studies that showed no association between social support (operationalized as receipt of social support from network members or perceived availability of support) and retention or linkage into care (Kelly, Hartman, Graham, Kallen, & Giordano, 2014; McCoy et al., 2009; Wohl et al., 2011). A retrospective study assessing RIC (assessed as two or more primary HIV visits in the 6 months before the study interview) in Latino and AA MSM and women found that receipt of social support from network members was not associated with RIC (Wohl et al., 2011). Similarly, a retrospective study on perceived availability of support and delay in linkage into HIV care found that social support (assessed by Medical Outcomes Survey [MOS]-Social Support questionnaire) was not related to linkage into care (McCoy et al., 2009). A prospective observational cohort study by Kelly et al. (2014) also found no association between perceived availability of support (assessed by MOS-Social Support) and RIC (assessed as having at least 1 visit for HIV care service in each of 3 or 4 quarter years in the year after diagnosis). Although it makes sense to think of social support as an antonym of social isolation, social support is a distinct concept that has constellations of types and definitions (i.e., tangible, emotional, functional, and structural, etc.). Thus, we cannot directly compare our findings to these study findings on social support and RIC, and future studies are needed to assess social support and indicators of social isolation on engagement in HIV care to adequately compare and evaluate the extent to which they are related to RIC and amongst each other. Furthermore, many of the

previous studies utilized different measures to assess RIC. Although there is no gold standard measurement for RIC (Mugavero et al., 2012) and a few studies report that some RIC measures are related to one another and its outcomes (Yehia et al., 2012; Mugavero et al., 2012), the relation of other RIC measures to appointment adherence is less understood in a sample containing primarily older PLWH. Incorporating additional measures of RIC such as visit constancy and gaps in care would be helpful in future studies examining RIC in older PLWH.

The lack of association between social isolation and RIC was unexpected because socially isolating environments or negative feelings of loneliness may be indicative of greater unmet needs and high levels of emotional strain, which may influence one's level of optimal adherence. In fact, many studies show significant association between social networks or social support and medication adherence in a sample with other chronic conditions and HIV/AIDS alike (Gallant, 2003; van Dam et al., 2005; DiMatteo, 2004; Magrin et al., 2015). The lack of association seen in our study could be due to many possible reasons: human behavior is complicated and may be altered by multiple factors. Social isolation may be too distal to affect RIC directly and that there may be more complex, mediating and moderating factors affected by social isolation, such as motivation, self-efficacy, and knowledge regarding clinical outcomes when a person is not retained in care (Jones, Cook, Rodriguez, & Waldrop-Valverde, 2013), that influence RIC. Furthermore, because RIC may require less effort than medication adherence (i.e., daily medication adherence vs. monthly or every few months appointment adherence), social isolation may have not influenced RIC to the extent that it affects medication adherence. Lastly, there may be system level and structural barriers that affect RIC that our study did not assess. A qualitative study (Yehia et al., 2015) involving a sample of 51 HIV-infected patients (age ≥18) recruited from Ryan White funded clinics has shown that an individual's

circumstantial factors (i.e., life activities and being acutely ill) and a clinic's structural factors (i.e., challenges with appointment scheduling, wait time, satisfaction with clinic or staff) affect one's level of engagement in HIV care. It is plausible that individuals may decide to not attend medical appointments, particularly those who may be economically disadvantaged and have less structured lifestyles, when there are competing life priorities. It is also likely that individuals may withdraw from care because appointment scheduling is inefficient and challenging to begin with. The quality of the service provided not only by the healthcare provider but also by the clinic staff may also affect appointment adherence. High rates of provider turnover may affect patient satisfaction (Reddy et al., 2015; Lam et al., 2016), which may in turn affect individual's continuity in care. A retrospective cohort study using Veterans Health Administration data found that primary care provider turnover was related to worse patient experiences (Reddy et al., 2015). Similarly, a few of our study participants verbally reported during the baseline assessment that they experienced issues with provider consistency that required them to re-establish rapport, which made them feel dissatisfied with the clinic. It is likely that these feelings of dissatisfaction related to provider turnover rates may affect appointment adherence. Future studies are needed to disentangle individual, interpersonal, and organizational/structural factors on RIC and Quality Improvement projects may be helpful in evaluating whether change in the environment and structure of the clinic system affects RIC in OPLWH.

Limitations

There are several limitations to this study that should be considered when interpreting the findings. First, our sample consisted of a purposive sample recruited from a clinic located in a large metropolitan area in the Southeast region of United States, which limits the generalizability

of our study results to the larger HIV population in the United States. Second, there may be other constructs that might be associated with RIC that we failed to control for. Also, this study focused on individual-level factors associated with RIC and did not assess broader factors related to the clinic or the services provided by the clinic that may affect RIC. Third, the recruiting clinic characteristics were stringent which may have affected RIC. For example, the clinic has a set of system where if patients were lost-to-follow-up for more than 6 months, they are automatically removed from the system and need to take on an arduous process to be re-enrolled back in to the clinic's system. This clinic characteristic may have affected the level of RIC in our sample. The recruiting clinic is a Ryan White funded clinic that provides integrated services to those who are socioeconomically disadvantaged. Integrated health services have been shown to be associated with improved engagement in care (Simeone, Shapiro, & Lum, 2017). The study findings may not be generalizable to those who may be more socioeconomically stable. Fourth, some participants are likely attend other outpatient clinics for HIV and other primary care services, those data were not captured. Individuals may also become incarcerated or institutionalized but still receive care outside of the recruiting clinic during the RIC data collection period. Therefore, we cannot assume those with suboptimal adherence were truly not receiving HIV care. It may be that some of the study participants utilize and receive health care services from clinics/hospitals other than our recruiting clinic. Fifth, this study excluded individuals who had never received HIV care since all participants were recruited directly from an outpatient HIV clinic. Findings should not be applied to those individuals who were never in HIV care or those who have been lost to follow-up. Furthermore, although we asked self-report of the number of years since being diagnosed with HIV, we were unable to capture year of entry into care. Many of our participants had been living with HIV for many years and may have been treated elsewhere before coming to

the recruiting clinic; their long period of having the disease and possible treatment duration may have affected more optimal integration with the healthcare system. Finally, we operationalized RIC using *appointment adherence* because it is more specific measurement of RIC that allows for assessment of relationships between correlating variables and RIC given our prospective study timeframe (Mugavero et al., 2010). Aging with HIV provides additional challenges and complexity to adequately define retention in care, since a typical HIV care encounter can also include are for other comorbidities. It was not always apparent if a visit addressed HIV issues specifically or other medical condition care visits when abstracting RIC data from EMR. Currently, there is no consensus on acceptable or clinically meaningful cut-offs for measures of RIC. The cut-off used in this study was developed specifically for this sample. Our clinical goal for this patient population is to achieve viral suppression and optimize CD4+ T cell count, and therefore a cut-off of 85% was utilized, based on our findings that this cutoff showed statistically significant differences on bassline viral suppression and CD4+ T cell count. Only baseline viral suppression and CD4+ T cell count (lab reports from ±2 months since the baseline visit) were available for our study and thus those were analyzed to select the cutoff. Further research is needed to determine if there are specific retention thresholds that can be predictive of poor clinical outcomes, especially with older PLWH who may require additional appointments for conditions other than HIV infection.

Our sample had an average of five appointments during the 12-month data collection period, which is higher than the recommended visit intervals for individuals with stable HIV infection (i.e., once per 6 months). Our sample of older PLWH may have been seeing their HIV care provider for management of other comorbid conditions and therefore have higher numbers of appointments than the recommended guideline. More research is needed to differentiate

between HIV care visits and other comorbidities care visits to enhance our understanding of RIC rates and clinical outcomes that incorporate both HIV and other comorbidities outcomes in older PLWH.

Conclusions

Our study is among the first to test the link between subjective and objective aspects of social isolation and RIC. The findings suggest that neither social network size nor loneliness was directly related to RIC. Emotion dysregulation was not associated with RIC but was related to both social network size and loneliness. One explanation for the lack of association is because social isolation may be too distal to affect RIC directly and that there may be more complex, mediating or moderating factors other than emotion dysregulation. Additionally, there may be system level and structural barriers that affect RIC that our study did not assess. Future studies are needed to disentangle individual, interpersonal, and organizational/structural factors on RIC.

Many sociodemographic factors and clinical characteristics including low income, problematic drug use, attitude towards HIV care team, detectable viral load, lower CD4+ T cell count, past homelessness, and acute hospitalization, were related to suboptimal RIC in our sample of older PLWH. Socioeconomically challenging environments such as unstable housing or homelessness and having no or low income may trigger a cascade of stressors that may serve as underlying risk factors for suboptimal RIC, including having to make a living to avoid financial obstacles and meeting basic needs as their first priority. Findings suggest that socioeconomic disparities and behavioral vulnerabilities including homelessness, low income, and substance use are closely linked to RIC among OPLWH. Future studies are needed to clarify RIC rates among those with current or past homelessness or with unstable housing and those

with socioeconomic and structural inequities, and to evaluate whether providing housing, telemedicine, or intensive outreach services might allow for better RIC and outcomes. Additionally, there is no consensus on acceptable or clinically meaningful cut-offs for appointment adherence especially with older HIV+ patients who may require additional appointments for conditions other than HIV infection. More research is needed to determine if there are specific appointment adherence thresholds that can be predictive of poorer clinical outcomes related to not only HIV infection and but also other comorbidities for these aging individuals who may be afflicted with many other health concerns.

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CHAPTER 5

SUMMARY AND CONCLUSIONS

Summary of Results

The present study assessed determinants of loneliness that may be uniquely present in older persons living with HIV (PLWH) and explored one potential mechanism by which social isolation (social network size and loneliness) may affect retention in care (RIC) via emotion dysregulation, using a modified Theoretical Model of Loneliness as a guiding framework (Hawkley & Cacioppo, 2010). The specific aims of the study were: 1) to assess the relationships of demographic factors, functional status, HIV-related stigma, HIV disclosure status, depressive symptoms, and social network size to loneliness in older PLWH and, 2) to assess the relationship of social isolation to emotion dysregulation and RIC in older PLWH on a proposed path model (**Figure 4.1**). Additionally, characteristics regarding suboptimal RIC among our sample were explored.

A cross-sectional, descriptive design was used to assess the relationship between correlates and loneliness. A descriptive, prospective component was used to assess the relationships among social isolation (loneliness, social network size), emotion dysregulation, and RIC. A purposive sample of older PLWH (age >=50) was recruited from a large outpatient HIV clinic located in the southeastern United States. Participants completed an in-person baseline study questionnaires. Clinical data (HIV biomarkers such as CD4+ T cell count and viral load, emergent health care utilization [HCU] such as emergency department [ED] visits and acute hospitalization) were collected via electronic medical record (EMR) abstraction. The lab values for HIV biomarkers reported within the closest time from baseline study visit were selected, not to exceed two months (i.e., the lab reports selected were ±2 months from the baseline visit).

Undetectable viral load was reported EMR lab value less than 40 copies/mL. RIC data were collected from EMR for 12 months post-baseline visit. A total of 146 participants were recruited and 144 participants had complete data on RIC. RIC was operationalized as *appointment adherence* and it was dichotomized into a binary outcome variable because this categorization better reflected HIV clinical outcomes: "optimal appointment adherence (>85%)" and "suboptimal appointment adherence (≤ 85%)."

The three manuscripts included in this dissertation describe the findings from the specific aims of this study and a systematic review on loneliness in older PLWH. To explore the current state of science in loneliness among older PLWH, a systematic review was conducted in **Chapter 2.** The review documents the significant gap in current understanding of loneliness in older PLWH, warranting the critical need for this dissertation research. The overall results of the studies indicate that demographics including older age, White race, Hispanic ethnicity, and male gender (Golub et al., 2010; Mannes et al., 2017; Han et al., 2017, Siconolfi et al., 2013; Vincent et al., 2017), HIV-related stigma (Vincent et al., 2017), substance use (Greene et al., 2018), unprotected sex (Golub et al., 2010), depression (Grov et al., 2017; Greene et al., 2018), and cognitive function (Han et al., 2017) are related to loneliness. Our study extends previous research findings by building a multivariate model that includes many of these correlates in relation to loneliness as an outcome.

The results of study aim 1 are found in **Chapter 3**. Approximately 41% of our participants scored 50 or greater on the loneliness scale, suggesting that this proportion of our sample had a higher than average score of the general population (Cella et al., 2010). This is not a surprising finding given the high prevalence of depression among older PLWH (Havlik, Brennan, & Karpiak, 2011) and the relationship between depression and loneliness (Grov et al.,

2010). Our finding is similar to a recent study that found a significant proportion of their sample of older PLWH reporting loneliness (Greene et al., 2018). The two-step hierarchical multivariable linear regression was conducted to identify the correlates of loneliness. In the first step, homelessness, comorbidity burden, and functional status were included. The second step considered study variables including HIV-related stigma, HIV-disclosure status, depressive symptoms, and social network size. The results of the first step showed that homelessness (β = 0.21, *p*=.007), comorbidity burden (β = 0.24, *p*=.002), and functional status (β = -0.18, *p*=.026) were significant correlates of loneliness and the model explained 15% of the variance in loneliness (R^2 = 0.15, F(3, 142)= 8.35, $p < .001$). In the second step, the addition of study variables in the regression analysis accounted for an additional 26% of the variance in loneliness, with the final model accounting for 41% of the variance in loneliness (R^2 = 0.41, F(7, 138)= 13.76, $p < .001$). Depressive symptoms (β = 0.35, $p < .001$) and HIV-related stigma (β = 0.29, $p < .001$) were significantly associated with loneliness in the final model, above and beyond the influence of non-modifiable factors such as past homelessness and disease status (i.e., comorbidity burden and functional status).

Finally, the results of study aim 2 are found in **Chapter 4**, which used path analysis to explore an *a priori* path model of social isolation on RIC directly or indirectly through emotion dysregulation, derived from a modified Theoretical Model of Loneliness (**Figure 4.1**). Social network size was added as an exogenous variable to our *a priori* path model to test the two aspects of social isolation simultaneously on RIC either directly or indirectly via emotion dysregulation. We first explored the differences in participant characteristics depending on their level of RIC. Of 144 participants, 81 participants had optimal RIC and 63 participants had suboptimal RIC. There were socioeconomic vulnerabilities and clinical characteristics that were

related to suboptimal level of RIC in our sample of older PLWH. Specifically, in a logistic regression, higher monthly income (B=0.80, p=.07), baseline CD4+ T cell count of ≥200 cells/mm^3 (B= 1.45, p=.05), and drug use (B=-0.28, p=.02) were significantly related to optimal RIC. For our path analysis, we hypothesized that both social network size and loneliness would have direct effects on RIC and also an indirect effect through emotion dysregulation among our sample of older PLWH. Fit indices reflected a good fit between the model and the sample data. The major findings from the path model, controlling for significant covariates, were three-fold: 1) neither loneliness nor social network size had a direct effect on RIC, 2) emotion dysregulation did not have a direct effect on RIC, and 3) both loneliness and social network size had direct effects on emotion dysregulation in our sample (**Figure 4.2**).

Research and Clinical Implications

The systematic review of the current literature showed that there are several gaps and challenges that warrant future research in loneliness among older PLWH. For example, some studies that were excluded from our review defined loneliness in terms of objective isolation (i.e., frequent social contact) or in combined subjective and objective isolation, thereby blurring the distinction between the two and complicating the interpretation of the findings. Furthermore, studies utilized different versions of the loneliness scale, preventing direct comparison of the findings. Future studies need to consider defining loneliness more descriptively and assessing the concept with a validated scale that is more commonly utilized among older PLWH (i.e., UCLA Loneliness Scale version 3). In addition, validated loneliness scales lack cut-points that signal the need for interventions or are predictive of clinical outcomes. Future research is needed to evaluate the cutoff points that can serve as a clinical indicator for interventions to prevent

negative health outcomes. Finally, more research is required to identify unique factors related to loneliness in order to identify targets for future interventions to reduce loneliness and prevent negative sequelae.

Our study findings contribute to understanding the factors related to loneliness. Loneliness was prevalent in our study sample. Assessment of loneliness using a brief screening tool may be important when someone is presented with symptoms of depression. Because loneliness is linked to HIV-related stigma and depression, it may be important to target these correlates to prevent or reduce loneliness. Past homelessness was associated with higher loneliness in our sample. Homelessness may disproportionately expose HIV-infected older individuals to additional stressors that may exacerbate feelings of loneliness and to prioritize of meeting basic needs rather than keeping HIV care appointments. Findings imply that targeting HIV-related stigma and depressive symptoms may reduce loneliness in older PLWH. Efforts to reduce stigma and depression in older PLWH are needed. Additional longitudinal research is also needed to evaluate the directionality of loneliness and depression and whether addressing loneliness may prevent depression or vice versa. Future research is needed to further establish determinants of loneliness and explore additional factors that may be predictive of loneliness in the older PLWH population. Other health outcomes known to be related to loneliness that were not explored in this study, including unprotected sex and cognitive function, should be explored in future studies, as well as prospective research to further confirm the causal influence of loneliness on health in older PLWH.

Our findings identified potential risk factors for suboptimal RIC in older PLWH. Past homelessness, lower CD4+ T cell count, lower monthly income, and drug abuse were related to lower odds of being in optimal RIC. Larger cohorts and prospective studies will allow for the

determination of causal relationships for more strategic and effective intervention or predictive model development. Our findings show that neither social network size nor loneliness directly or indirectly influence RIC. Future studies are needed to disentangle individual, interpersonal, and organizational/structural factors on RIC. Our sample had an average of five appointments during the 12-month data collection period, which is higher than the recommended visit intervals for HIV monitoring (once every 6 months) from the established guidelines for stable HIV+ patients (Department of Health and Human Services [DHHS], 2018). This may be due to this sample having more comorbidities that require management of other chronic conditions in addition to HIV infection. In fact, our sample had comorbidity burden ranging up to eight (median=1).

Future studies are needed to tease out visits for HIV monitoring versus visits for HIV '*plus'* other comorbidity monitoring, and to evaluate how either of or incorporation of both care encounters affect HIV and comorbidities outcomes. In addition, there is no consensus on an acceptable or clinically meaningful cut-point for appointment adherence as a measure of RIC. We chose a cut-off of 85% because it showed statistically significant differences on baseline viral load and CD4+ T cell count. We were not able to collect long-term HIV biomarkers because of our study design and purposes, so we were unable to evaluate the prognostic value of this cutoff in predicting viral suppression and optimal CD4+ T cell count. Future studies are needed to determine if there are specific RIC thresholds that are predictive of poorer clinical outcomes related to not only HIV but also with other chronic conditions (i.e., diabetes, hypertension, etc.). Consensus is required on the recommended visit interval to tailor HIV and chronic condition management in older PLWH who may be living in socially and financially challenging environments.

Limitations

This study should be considered within its limitations. The cross-sectional design precludes inferences about causality. Generalizability may also be limited since our sample was predominately male, black/African American (AA) race, heterosexual, and had been living with HIV for many years. However, some of these characteristics are similar to the current HIV epidemic in the South, which indicates predominant rates of HIV infection in males and AAs (CDC, 2017). Although our sample consisted of individuals self-reporting as primarily heterosexuals, which is unlike that of the current HIV prevalence estimates in the United States, our sample reflects the clinic's patient population characteristics. As such, our findings may not be generalizable to those who are not heterosexual. The temporal effects of loneliness were not assessed and therefore future studies should utilize longitudinal designs to assess for changes and causal relations in loneliness and its related factors. There may be other constructs that might have been associated with RIC that we failed to control for. Also, this study focused on individual-level factors of RIC and did not assess broader factors related to the clinic or the service provided by the clinic that may affect RIC. The current study data were collected from a purposive sample of older PLWH attending a comprehensive HIV care clinic in a high resource setting. The recruiting clinic is a Ryan White funded clinic that incorporates a "one-stop shop" type of practice and provides integrated health services including psychiatric (group therapy and individual sessions), pharmacy, dental, and primary medical care services. Integrated health services have been shown to be associated with improved engagement in care (Simeone, Shapiro, & Lum, 2017). The clinic not only provides medical support but also allows patients to

engage in social activities. In addition, the clinic has a set of systems that imposes a laborious process of re-enrollment if patients are lost-to-follow-up for more than 6 months. Therefore, the characteristics of the clinic may have affected our sample's social network size and its influence on loneliness, and the level of RIC in our sample, limiting generalizability. This setting and sample may not be a representative sample of the general HIV-infected population, and may suggest the possibility of even worse loneliness and RIC in resource limiting settings. Accordingly, many factors in the current study may not be applicable to the general HIV population or those who are much more vulnerable such as those who are socially disenfranchised or lack access to care/resources such as those in rural areas. Individuals may also become incarcerated or institutionalized but still receive care outside of the recruiting clinic during the RIC data collection period. Therefore, we cannot assume those with suboptimal adherence were truly not receiving HIV care. It may be that some of the study participants utilize and receive health care services from clinics/hospitals other than our recruiting clinic. Despite these limitations, this study contributes to the literature by explaining contributing factors to loneliness and characterizing older PLWH who may be sub-optimally retained in care. These characteristics may allow for targeting or adapting interventions more appropriately in reducing loneliness and improving retention in care. The study also explored one mechanistic pathway of how RIC might be affected, which showed non-significant findings and suggests complex mechanism of RIC. Future studies should explore more complex modeling with utilization of larger dataset.

Conclusions

Loneliness is a common problem among older PLWH. Research on the psychosocial context of older PLWH has increased recently and loneliness is deemed an important factor that may affect the health and lives of older PLWH. The current study assessed contributing factors to loneliness and tested the link between social isolation and RIC in a sample of older PLWH. The results suggest that a meaningful proportion of our sample of older PLWH experience loneliness, and that depression and HIV-related stigma explain a significant amount of loneliness in our sample of older PLWH. These findings therefore imply that targeting HIV-related stigma and depressive symptoms may reduce loneliness in older individuals diagnosed with HIV. Considering the potential for preventing some clinical outcomes related to loneliness, screening for loneliness in clinic settings may be beneficial. Additionally, the findings suggest that neither social network size nor loneliness was directly related to RIC. Emotion dysregulation was not associated with RIC but was related to both social network size and loneliness. Many sociodemographic factors and clinical characteristics including low income, problematic drug use, lower CD4+ T cell count, and past homelessness were related to suboptimal level of RIC in our sample of older PLWH. Findings suggest that social determinants of inequities such as homelessness and substance use are closely tied to RIC among older PLWH.

Future studies are needed to disentangle individual, interpersonal, and organizational/structural factors on RIC and to address the effects of current or past homelessness or unstable housing on RIC rates. Additional qualitative, quantitative, and mixed-methods studies may broaden our current knowledge of social isolation in this population. Future studies should also consider investigating the association between living arrangements and social

isolation, such as geographic arrangements including rural or urban environments, and living environments like nursing homes, residential homes, or half-way houses. Longitudinal research on social isolation among older PLWH is warranted to investigate the temporal effects of social isolation as well as to examine potential mechanisms and causal pathways that link social isolation and health of older PLWH to better inform efforts to improve well-being among this patient population.

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