The Association Between HIV-Stigma and Depression Among South African People Living with HIV/AIDS: A systematic Review

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Abstract

Background and Aims: Across the globe, HIV/AIDS is one of the most pressing public health concerns. People living with HIV/AIDS (PLWHA) are at increased risk of mental health difficulties, and this appears to be a particular issue in South Africa, which is home to almost 20% of the world's HIV-positive population. Recent research has sought to develop our understanding of the relationship between HIV-stigma and depression in South Africans, however the research remains fragmented and vulnerable groups have often been overlooked (e.g., adolescents). This study aimed to systematically review the literature investigating the relationship between HIV-stigma and depression amongst PLWHA in South Africa.

Methods: Four bibliographic databases (CINAHL, Ovid MEDLINE, PsycINFO, and Web of Science) and three grey literature websites were systematically searched using different keywords to obtain relevant studies from 1997 to 2019. Reference lists of relevant studies were also searched. Studies were eligible for inclusion if they were written in English, assessed levels of depression and HIV-stigma amongst a sample of HIV-positive South Africans, and attempted to measure a relationship between these outcomes. Data was extracted from eligible studies using a pre-designed template produced for this review and the quality of these studies was assessed. A qualitative synthesis was conducted in order to determine the prevalence of HIV-stigma and depression, potential relationships between these measures, and to identify any mediators or moderators of this relationship.

Results: Fourteen quantitative studies were included in the review, of which two were prospective cohort studies and twelve were cross-sectional. Five studies were determined to be of high quality, eight were fair quality, and one was low quality. PLWHA in South Africa experience high levels of HIV-stigma and depression. All forms of stigma were found to be associated with depression amongst PLWHA, however each association appears to be unique. Prospective findings were mixed, with one study finding that stigma did not predict depression over time, and another found that depression predicted stigma 12 months later, suggesting a potentially bidirectional relationship. Females and adolescents appear to be particularly vulnerable to HIV-stigma and its negative psychological effects. Social support was determined not to be a consistent mediator or moderator of this relationship across different sub-populations of PLWHA.

Conclusion: There appears to be a consistent cross-sectional relationship between all forms of stigma and depression amongst PLWHA in South Africa, yet the true extent of this relationship, including the role of social support, remains unclear. Future research must endeavour to fully understand this complex relationship through stronger study designs, the assessment of potential mediators/moderators, and the inclusion of various sub-populations of PLWHA (e.g. adolescents).

1. Introduction

1.1 *Contextualising the HIV Epidemic*

HIV/AIDS represents one the most significant public health concerns, the world over. Human immunodeficiency virus (HIV) fights the body's immune system, specifically combatting CD4 cells which support the body in fighting against infection (U.S. Department of Health and Human Services (HHS), 2019), and, if left untreated, the virus can lead to acquired immunodeficiency syndrome (AIDS). Whilst, to date, no cure for HIV has been developed, the advent of Antiretroviral Therapy (ART) in 1984 and Highly Active Antiretroviral Therapy (HAART) in 1996 has resulted in a significant reduction of morbidity and mortality rates over the past several decades (Maartens, Celum & Lewin, 2014). Despite this, prevalence rates are high and adverse effects are synonymous with being HIV-positive (HHS, 2019). According to the WHO (2019), by 2017 there were 36.9 million people living with HIV/AIDS (PLWHA) worldwide. Furthermore, since the beginning of the epidemic over 70 million people have been diagnosed with HIV and approximately 50% of these cases have resulted in premature mortality (WHO, 2019).

Despite the majority of current HIV knowledge and research stemming from high-income countries (HICs), global prevalence rates of the infection have long been extremely imbalanced, and tip towards low- and middle-income countries (LMICs) (Collins et al., 2006). Specifically, whilst being home to a mere 12% of the world's population, countries in Sub-Saharan Africa are cumulatively home to around 71% of all PLWHA and up to 90% of all HIV-infected children (UNAIDS, 2019). The aforementioned imbalance in HIV prevalence is also evident within this region as, of those cases in Sub-Saharan Africa, 25% emerge from South Africa (SA) (UNAIDS, 2019). Furthermore, in 2010 HIV/AIDS contributed 39.9% of all disability-adjusted life years (DALYs) (Ortblad, Lozano, & Murray, 2013) and 47.9% of years of life lost to disability (YLL) in South Africa (Institute for Health Metrics and Evaluation (IHME), 2010). Whilst these statistics have decreased in recent years, HIV remains the leading cause of disability and premature death (IHME, 2019). Moreover, South Africa is, in global terms, home to the most substantial HIV epidemic – representing 19% of all PLWHA (UNAIDS, 2019). It is proposed that these figures are powered by both biological and social factors, including high rates of gender-based violence; low levels of education; high unemployment rates; and mental and physical healthcare challenges (Centre for Strategic and International Studies (CSIS), 2019). Moreover, having peaked in 2013, global spending on HIV in Sub-Saharan Africa has substantially declined, thus exacerbating the issues contributing towards the epidemic (IHME, 2019). Conversely, HIV has had a substantial negative impact upon Africa's economic growth and, therefore, its capacity to manage the condition (Dixon, McDonald & Roberts, 2002).

1.2 *Stigma and HIV-stigma*

The *Global Network of People Living with HIV/AIDS* cite stigma and discrimination as one the most pervasive challenges PLWHA face (2019). Stigma is defined as a 'marker', which indicates to others that the bearer is 'tainted', or 'sub-human' (Pescosolido, 2013). The concept may be divided into three categories: 'public-stigma' (awareness of negative attitudes held by the general population (Quinn & Earnshaw, 2014)); 'internalised-' or 'self-stigma' (the application of these attitudes towards the self (Corrigan & Watson, 2002)); and 'structural-stigma' (the influence of negative attitudes at the institutional level, reflecting economic and political forces (Corrigan, Markowitz & Watson, 2004)). Despite an increasing awareness of the mechanisms underlying stigma, our knowledge of the aforementioned phenomena is limited by their cross-cultural complexity (Pescosolido, Olafsdottir, Martin & Long, 2008). As Kramer and colleagues (2002) note, whilst stigma has been demonstrated across every culture, it manifests uniquely depending upon a complex array of cultural and contextual factors. Recent stigma research has therefore advocated for the development of a research base which accounts for these factors within specific contexts (e.g., Pescosolido, Olafsdottir, Martin & Long, 2008).

According to Parker and Aggleton (2003), HIV is one of the most stigmatised diseases in history. Within the context of HIV, stigma may be best understood as a combination of 'enacted' stigma (discrimination experienced by PLWHA), 'anticipated' stigma (the knowledge that negative attitudes exist towards HIV and the expectation that the PLWHA will experience prejudice and discrimination at some point), and 'internalised' stigma (direction of negative societal attitudes towards the self) (Thomas et al., 2005). That is to say, for PLWHA, the awareness that HIV is a societally-devalued attribute may manifest in numerous ways, through direct experiences of prejudice or discrimination; anticipating discrimination; or viewing themselves negatively (Earnshaw & Chaudoir, 2009). As mentioned previously, this is a globally stable finding, yet it is those residing in low- and middle-income countries (LMICs) who appear to be at greatest risk (Mascayano, Armijo, & Yang, 2015). A recent review conducted by Lowther, Selman, Harding, and Higginson (2014) found prevalences of HIV-stigma in PLWHA to be between 42% and 46% in HICs and up to 82% in LMICs. This is particularly true for countries in Africa, where HIV prevalence rates are the highest in the world. For example, a recent review conducted by Mbonu, Van den Borne, and Vries (2009) demonstrated consistently high and pernicious levels of HIV-stigma across Sub-Saharan Africa, which were associated with complex mental health outcomes.

1.3 *HIV and Mental Health*

Beyond the physical symptoms associated with HIV/AIDS, a growing body of evidence suggests that PLWHA are at increased risk of mental health issues (Prince et al., 2007). The direct impact of HIV upon the brain and the psychosocial impact of living with the condition are widely acknowledged determinants of mental illness amongst this population (Treisman & Kaplin, 2002). In terms of neurobiology, HIV/AIDS instigates changes which damage the central nervous system (CNS) and

produce complex cognitive deficits (Dubé, Benton, Cruess, & Evans, 2005). Moreover, PLWHA face high rates of psychosocial stress, such as that associated with poverty, poor social support, and stigma and discrimination (Heckman, 2003). As a consequence of these biological and psychosocial stressors, mental health conditions are the most common comorbidities associated with being HIV-positive and are disproportionately high in PLHWA in comparison to the general population (e.g. Chibanda, Benjamin, Weiss, & Abas, 2014). This is particularly true for those living in LMICs, where, in some cases, prevalence rates of depression were found to be double that of non-infected controls (e.g., Adewuya et al., 2007). Furthermore, anxiety symptoms vary between 9% and 34% in PLWHA in Sub-Saharan Africa, in comparison to between 3% and 7% of the general population (Baxter et al., 2014).

Depression, however, is the most common mental disorder amongst PLWHA, with prevalences ranging from between 14% and 32% (Bernard, Dabis, & De Rekeneire, 2017). Even in cases where individuals do not meet criteria for a depressive disorder, depressive symptoms have been associated with adverse health outcomes, including accelerated progression of symptoms, lower CD4 cell counts, and reduced life expectancy (e.g. Ironson et al., 2005). Moreover, it is well documented that those with comorbid HIV and depression are less likely to adhere to ART (Waldrop-Valverde & Valverde, 2005; Uthman, Magidson, Safren & Nachega, 2014) and this finding is consistent even at non-clinical levels (Gonzalez, Batchelder, Psaros & Safren, 2011). Research demonstrates that PLWHA who have depression are also more likely to engage in unsafe sexual practices (e.g., Musisi et al., 2014), alcohol abuse (e.g., Fisher, Bang & Kapiga, 2007), and illicit drug use (e.g., Cook et al., 2007), which increase the likelihood of HIV-transmission and accelerated disease progression. Considering that by 2030 both HIV/AIDS and depression are expected to be the greatest contributors towards years lived with disability (YLD), worldwide (Mathers & Loncar, 2006), it is essential that research aims to more fully understand the relationship between these two factors.

1.4 *HIV-Stigma and Depression*

Research suggests that, given its far reaching social and psychological effects, HIV-stigma is a key contributing factor towards adverse mental health outcomes in PLWHA (e.g., Herek, Saha & Burack, 2013). Studies have consistently demonstrated positive relationships between HIV-stigma and mental health issues such as anxiety (Vance, 2006), reduced quality of life (Vyavaharkar et al., 2011), suicidal ideation (Capron et al., 2012), and stress (Siegel, Lekas, & Schrimshaw, 2005). It is suggested that the negative attitudes and discrimination associated with the possession of a stigmatized trait interfere with countless areas of an individual's life such as relationships, employment, and wellbeing (Roeloffs et al., 2003), and this is particularly true for those living with HIV who experience some of the highest levels of stigma, the world over (Parker & Aggleton, 2003).

Those living with HIV are challenged doubly, as they simultaneously live with the physical challenges associated with their illness as well as stereotypes and prejudice which result from misconceptions of HIV (Corrigan & Watson, 2002). For example, PLWHA are victims of the 'fear of contagion' whereby individuals believe that HIV may be transmitted via casual contact and, hence, they become isolated (Sayles et al., 2007). Moreover, these individuals are often inflicted with blame and punishment for their diagnosis, and this occurs in culturally meaningful ways (Smith & De Santis, 2012). A study conducted in South Africa, for example, demonstrated that adolescents anticipated being stigmatized by community members as 'punishment from God or ancestors' (Pantelic, Boyes, Cluver & Thabeng, 2018, p. 213). The resultant discrimination and social isolation of HIV-stigma, hence, have a detrimental impact upon the mental health of PLWHA, and depression is a poignant example of this (Endeshaw et al., 2014).

A substantial body of research has found depression to be the most common outcome of stigma directed towards PLWHA (e.g. Brandt, 2009). For example, Murphy, Garrido-Hernansaiz, Mulcahy, and Hevey (2018) determined HIV-related stigma to be the most significant predictor of depression in their HIV-positive sample. This relationship may manifest as a direct result of the aforementioned social isolation and stressors imposed upon PLWHA or through indirect effects. For example, PLWHA face high levels of stigma in healthcare settings which often results in the denial of treatment and care, humiliation, and confidentiality breaches (Elford et al., 2007). Similarly, anticipated- and self-stigma can result in reduced help-seeking behaviours or treatment adherence (Teh, King, Watson & Liu, 2014), as well as lowered self-esteem (Kalomo, 2017). The relationship between HIV-stigma and depression is, hence, complex and multifaceted, and this contributes massively towards the current dearth of effective interventions to combat stigma's adverse effects (Sengupta et al., 2011).

1.5 *Current Systematic Reviews*

There are several systematic reviews which have investigated similar questions pertaining to HIV-stigma and depression. Both Breuer and colleagues (2011), and Brandt (2009) reviewed literature which has investigated the relationship between HIV/AIDS and mental and physical health in Sub-Saharan Africa. In addition, Rueda and colleagues (2016), did so with studies assessing the association between HIV-stigma and general health in HICs and LMICS. Each of these reviews demonstrated evidence for a relationship between HIV-stigma and depression. Breuer and colleagues (2011), for example, demonstrated that high levels of depression were mainly explained by high levels of stigma, and suggested that social support may play a role in this relationship. Moreover, Brandt (2009) found that internalised stigma was the greatest predictor of depressive symptomology amongst both male and female samples. Similar to the findings of Breuer and colleagues (2011), Rueda and colleagues (2016) suggested that the positive relationship between HIV-stigma and depression may be mediated by levels of social support. Despite these findings, these reviews have several important limitations.

Breuer and colleagues (2011), and Brandt (2009) both investigated all factors which may have contributed towards adverse mental and physical health outcomes amongst PLWHA. Hence, very few of the included studies looked specifically at stigma and its relationship to depression, or depressive symptoms. Despite the fact that both reviews concluded that stigma was an important determinant of adverse mental health outcomes, such as depression, we are unable to fully appreciate the extent of the relationship between HIV-stigma and depressive symptoms, particularly the impact of specific forms of stigma. Moreover, both excluded studies which sampled from beyond general HIV-positive adults. Hence, their findings cannot be generalized to other populations of PLWHA such as adolescents or pregnant women. This is significant as, whilst global infection and premature death tolls have steadily declined, child and adolescent HIV statistics remain alarmingly high. Female adolescents, for example, account for 25% of all new infections in Sub-Saharan Africa, despite representing a mere 10% of the population (the Lancet, 2018). African Adolescents living with HIV have been evidenced as being at greater risk of HIV-stigma and depression than infected adults (Ashaba et al., 2018). As adolescence is a key developmental stage with significant potential in terms of preventing adverse physical and mental health outcomes in later life, it is fundamental that this population are represented within the literature (Pettifor, Stoner, Pike, & Bekker, 2018). In addition, research has demonstrated that pregnant women (e.g., Cuca, Onono, Bukusi & Turan, 2012) and mothers (e.g., Turan et al., 2011) are more likely to experience HIV-stigma and depression than the general HIV-positive population, yet little research has attempted to understand the relationship within this at-risk sub-population (Turan et al., 2011).

Intervention studies targeting different sub-populations have consistently identified a lack of comparative measures and data from across studies as halting the development of accurate interventions to improve wellbeing (e.g. Pulerwitz, Michaelis, Verma, & Weiss, 2010). Hence, it is essential that reliable studies and reviews investigating the relationship between HIV-related stigma and depression in these vulnerable HIV-positive populations be conducted. Rueda and colleagues (2016) produced a more in-depth investigation of HIV-stigma and its relationship with mental health, with findings suggesting that HIV-stigma was most highly associated with increased levels of depression, lower social support, and lower ART adherence. Yet, of the sixty-four studies included, only fourteen were conducted in LMICs, and a mere six of these were in Sub-Saharan Africa. Furthermore, despite collecting data regarding the relationship between mental health outcomes and numerous forms of stigma (internalised, anticipated, and enacted), the stigma measures were aggregated to simply refer to 'HIV-stigma'. Hence, we are unable to determine how these different forms of stigma relate to depression, as well as to one another.

Thus, current research has demonstrated a relationship between HIV-stigma and depression, yet the reviews do not conduct in-depth analyses of this relationship and often exclude or do not focus on vital populations, such as Sub-Saharan Africans or adolescents. Furthermore, as Brandt (2009, p. 124) notes,

despite an increase in the number of studies conducted Sub-Saharan Africa, "the body of research remains fragmented and the methodological quality is uneven. Consequently, not all the findings can be considered equally robust and their comparability is limited." Therefore, it is essential that we attempt to bring this often-fragmented research together, and to review the nature and quality of it.

1.6 *Summary and Aims*

Individuals living with HIV/AIDS are likely to face a myriad of physical and mental health challenges which are exacerbated by the stigma that they face as a result of their diagnosis. They are at particular risk of depression which not only impacts the individual's quality of life, but can worsen the symptoms, progression, and spread of HIV. Moreover, whilst almost 20% of the world's HIV-positive population reside in South Africa, there is a dearth of research investigating HIV-stigma and its effects within this context. Recent systematic reviews have explored the relationship between HIV-stigma and depression, but have not done so in depth and have often overlooked particular populations, including Africans and adolescents.

The aim of this current study is to conduct the first comprehensive systematic review of research investigating the relationship between HIV-stigma and depression amongst PLWHA in South Africa. In light of the fact that stigma is experienced in different ways and at different rates depending upon the particular sub-population of PLWHA (e.g., Ashaba et al., 2018; Turan et al., 2011) this review shall investigate the relationship between HIV-stigma and depression within different HIV-positive samples. More detailed examination of these relationships may be of benefit to researchers and policymakers who rely upon in-depth, empirical research in order to produce effective interventions and policies which target at-risk populations.

The aims of this study are threefold: (1) to determine the prevalence of HIV-stigma and depression amongst PLWHA in South Africa; (2) to assess the relationship between HIV-stigma and depression amongst different sub-populations of PLWHA in this region; and (3) to identify potential moderators and mediators of this relationship.

2. Methods

2.1 *Search strategy*

This systematic review was conducted in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-Analyses' (*PRISMA statement*; Moher, Liberati, Tetzlaff, & Altman, 2009). The search strategy was determined by the author and reviewed independently by an additional researcher (AF). Any resultant discrepancies were resolved through discussion. In order to identify relevant

studies electronic databases and grey literature websites were searched. The search was restricted to publications produced between January 1st, 1997 and April 26th, 2019. Studies prior to 1997 were excluded as this was the year that highly active antiretroviral therapy (HAART) became the standard treatment for HIV and AIDS-related deaths reduced significantly (CDC, 1997). Thus, HIV/AIDS began to be understood as a treatable condition and HIV-stigma gained more attention within research (e.g. Brandt, 2009). A grey literature search of two websites (OpenGrey and OAIster) was conducted in an attempt to minimise potential publication bias of the review (Paez, 2017). Four bibliographic databases (CINAHL, Ovid MEDLINE, PsycINFO, and Web of Science) were selected in order to identify literature within the fields of medicine, nursing and psychology. For each database, specific MeSH and keyword terms were employed for HIV/AIDS, HIV-related stigma, and Depression (see Appendix 1), and an exemplar search strategy can be viewed in Appendix 2. Having piloted search terms relating to South Africa, results depleted substantially and, hence, they were not included in the final search. This is consistent with several existing systematic reviews investigating similar topics (Brandt, 2009; Breuer, Myer, Struthers, & Joska, 2011). The Cochrane Database of Systematic Reviews was also searched. Studies found in the reference lists of included studies were additionally assessed for eligibility.

2.2 *Eligibility Criteria*

Studies were eligible for inclusion if they were written in English, quantitatively measured levels of depression and HIV-stigma amongst an HIV-positive sample, of any age, living in South Africa, and reported on a statistical test for the relationship between these measures. This included quantitative and mixed-method studies, as well as psychometric studies validating measurements of HIV-stigma.

The exclusion criteria included studies that did not directly report the relationship between depressive symptoms and HIV-stigma, this included qualitative designs, intervention trials (unless analyses were reported from data taken at baseline) and case studies, as well as articles. Qualitative studies were excluded as it has previously been noted that a lack of reliable quantitative research has halted the development of accurate anti-stigma interventions. Hence, it is important to understand what future quantitative research needs to do in order to rectify this. Studies were excluded if they only measured stigma-by-association in HIV-negative individuals (e.g. those orphaned by HIV/AIDS or living with an HIV-positive caregiver) as their experiences of HIV-stigma may be different to those with the disease, and it is not fully understood to what extent the effects of HIV-stigma are shared amongst these populations (Wight et al., 2006). This exclusion criteria is consistent with similar reviews (e.g., Lowther et al., 2014; Rueda et al., 2016).

2.3 *Study Screening*

The study identification and screening process can be viewed in Figure 1. In accordance with the Cochrane Collaboration Handbook (Deeks, Higgins, & Altman, 2008) results from the database search (n=1459), grey literature (n=4) and reference-list search (n=1) were combined in EndNote and duplicates were removed (n=539). Titles and abstracts were screened as an initial stage, and irrelevant articles were removed (n= 830). Full text articles were then retrieved and assessed for compliance with inclusion and exclusion criteria (n=95). Of these articles; forty-nine did not include a South-African sample; nine did not quantitatively assess level of depression; four lacked a stigma measure; nine did not measure the relationship between these measures; and ten did not include an HIV-positive sample (∑n=81). Of the studies found in the grey literature search (n=4), zero were eligible for inclusion as they did not include an HIV-positive sample (n=2), did not measure levels of depression (n=1), or did not assess the relationship between these measures (n=1). One study (Wingood et al., 2008) was identified through reference-list search and was eligible for inclusion in the final review. Once screening was completed, the final review was composed of fourteen studies.

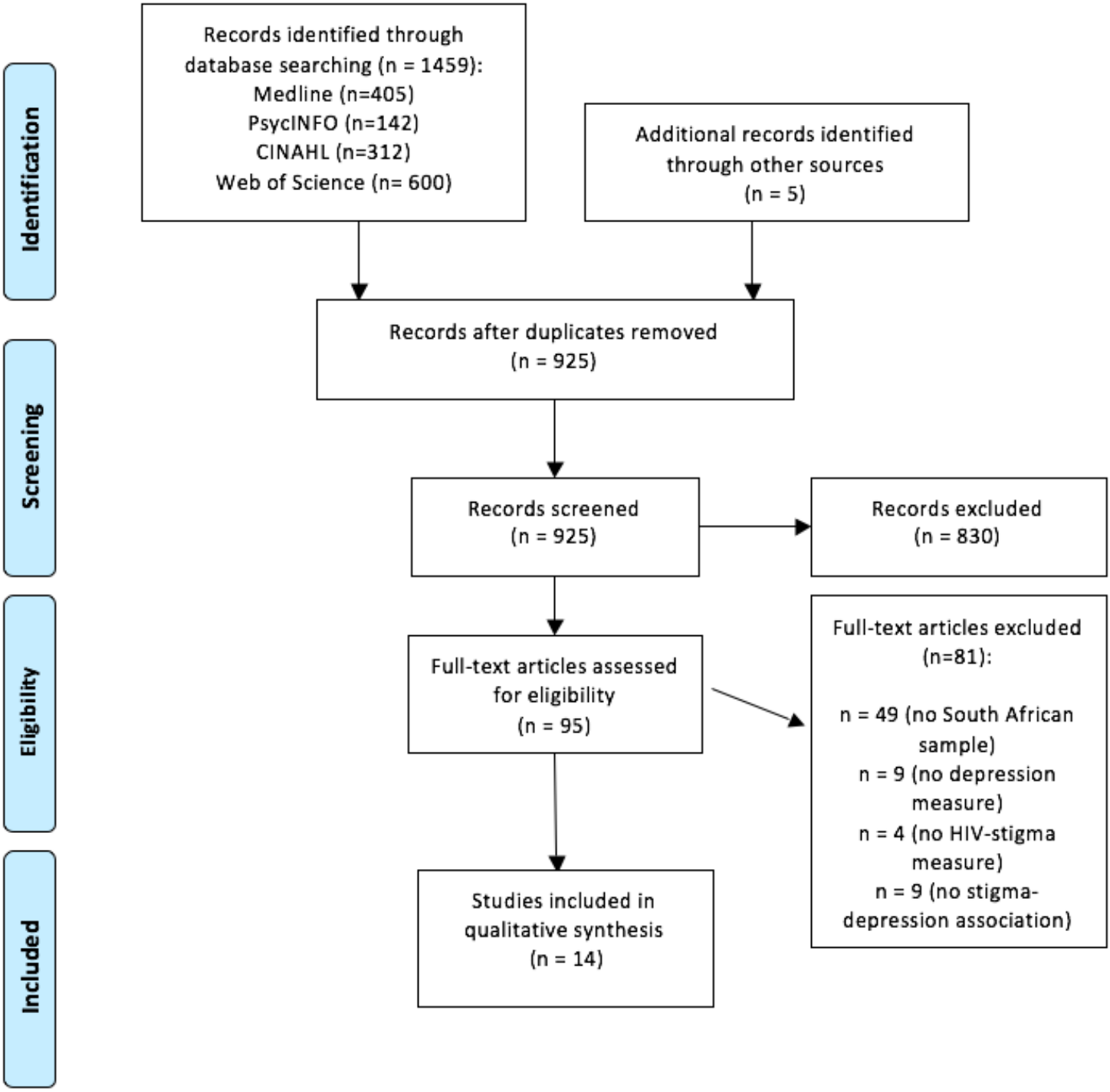

Figure 1: PRISMA flow diagram of study identification and Selection Process

2.4 *Data Extraction and Quality Assessment*

Data for the included studies was extracted into a pre-designed template, produced for this study (Appendix 3). Once again, the data extraction template and quality assessments were reviewed by another researcher (AF) and disputes were resolved by discussion. For each study, extracted data was separated into five main subsections; study and design (title, authors, year, publication journal, aims, and study design), sample (size, gender composition, region of South Africa, clinical/community, mean age, additional demographic information (e.g. rural/urban residence, education etc.)), recruitment method (inclusion/exclusion criteria, facility and within-facility sampling technique (for clinical samples)), and methodology (stigma/depression measures and validity and additional psychological measures). The final subsection was dedicated to main results and authors' interpretations of their findings.

Quality of included cross-sectional studies (n=12) were appraised using Pantelic and colleagues' (2015) adaptation of the *Cambridge Quality Checklist* (CQC; Murray, Farrington, & Eisner, 2009), which was used to assess studies which measured the association between internalised HIV-stigma amongst Sub-Saharan African samples (Appendix 4 (i)). This adaptation was modified to include assessment of each study's depression measure. Furthermore, an assessment of each study's attempt to control for confounding variables was added to appreciate, more fully, the reliability of the included measures. This adapted version of the CQC includes a comprehensive appraisal of recruitment method (facility and within-facility), sample (e.g. response/retention rates and sample size), and methodology (measure validity/reliability, study design, and analysis type). Studies were graded on a numerical scale and a final score was produced based upon a percentage of a possible 24 points. Pantelic and colleagues' (2015) adaptation of the CQC was conducted in order to assess quality of reporting and methodology within Sub-Saharan African studies, specifically. In doing so, they included method of selection of facilities, and participants within facilities to account for the fact that studies conducted in this region tend to recruit through health-care settings (Pantelic et al., 2015). Hence, this assessment tool is applicable to the target population. Cohort studies (n=2) were assessed using the *Newcastle-Ottawa Quality Assessment Form for Cohort Studies* (Wells et al., 2008; Appendix 4 (ii)). The tool appraises cohort studies based upon quality within three broad areas; study-group selection; comparativeness of the cohorts; and assessment of the outcome; and rates studies based upon a star system. Following the approach of each tool's authors (which can be found in Appendix 4), studies were categorised as high, fair or low quality.

3. Results

3.1 *Study Characteristics*

A summary of the sample characteristics, study design, measures, key findings and quality assessment of each of the fourteen included studies are grouped chronologically and presented in Table 1. The studies are geographically representative; including fourteen unique samples from Mpumalanga, the Western Cape, KwaZulu-Natal province, the Eastern Cape, Free State province, and Johannesburg, cumulatively involving 9,843 PLWHA. All studies were quantitative, of which twelve were cross-sectional and the remaining two were prospective cohort studies (PCS). The majority of studies included adult samples (n=6), of which three included adults initiated on ART (Peltzer & Ramlagan, 2011; Pappin, Wouters, & Booysen, 2012; Wouters, Masquillier & Booysen, 2016), one included adults experiencing chronic pain (Wadley, Pincus, & Evangeli, 2019), one included HIV-positive women (Wingood et al., 2008), and one included a racially diverse sample (Simbayi et al., 2007). The remaining studies sampled pregnant women, (n=2), mothers (n=2), and adolescents (n=3). Several studies measured multiple types of stigma, including internalised stigma (n=9), external stigma (n=4), and perceived stigma (n=1). Five studies also included a general measure of HIV-stigma. The majority of studies recruited participants through healthcare facilities (n=11). The remaining three recruited through community organizations (Breet, Kageea, & Seedatb, 2014; Gamarel et al., 2017), or through both healthcare and community settings (Pantelic et al., 2017).

3.2 *Validity of Included Measures*

As previous research has highlighted heterogeneity of measures across studies within this context (Brandt, 2010) and critiqued the use of 'Western' assessment tools (e.g., Alarćon, 2009), it is important to assess the cross-cultural validity of those included within the studies of this review.

Across the fourteen studies, measures of stigma were somewhat heterogeneous. The most common measure was the *Internalized AIDS-related stigma scale* (IA-RSS, Kalichman et al., 2009) which was validated with a South African population and was included in four studies (Simbayi et al., 2007; Peltzer & Shikwane, 2011; Peltzer & Ramlagan, 2011; Valerie, Earnshaw, Kidman, & Violari, 2018). Two studies utilized the *HIV-stigma Scale* (Berger, Ferrans & Lashley, 2001) which measured overall stigma score and, similarly, has been validated within Sub-Saharan African contexts (Wingood et al., 2008; Breet, Kageea, & Seedatb, 2014). Wouters, Masquillier and Booysen (2016) used an adapted and non-validated version of the *HIV-stigma Scale* (Wright et al., 2006). Two studies (Pantelic et al., 2017; Casale et al., 2019) assessed stigma using the adapted *Adolescents Living with HIV Stigma Scale* (ALHIV-SS; Pantelic et al., 2016), which assesses levels of internalised and enacted stigma was developed for adolescents living in the US, adapted for South African participants by Pantelic and colleagues (2018), and validated by Casale and colleagues (2019). Two studies (Brittain et al., 2017;

Wong et al., 2017) used an adapted version of the *Social Impact Scale* (Fife & Wright, 2000), which is yet to be validated amongst African samples. This measure assesses levels of internalised and enacted stigma. One study (Wadley, Pincus, & Evangeli, 2019) included the *HIV/AIDS Stigma Instrument - PLWHA* (HASI-P), which measured levels of enacted and internalised stigma and has been validated by Holzemer and colleagues (2007). The remaining studies all included non-validated measures of HIV-stigma, such as the *USAID Self-Stigma Scale* (USAID, 2006) used by Gamarel and colleagues (2017) and Pappin, Wouters, and Booysen's (2012), *Stigma Scale* which was composed of eight questions relating to levels of internalised and anticipated stigma.

In terms of depression measures, the studies were more homogenous and each scale had been previously validated with populations from Sub-Saharan Africa. These include the *Edinburgh Postnatal depression scale* (EPDS; n=3), the Centre for Epidemiological studies Depression scale (CES-D; n=4), the Child's Depression Inventory (CDI; n=2), the Beck Depression Inventory (BDI; n=3), and the Hospital Anxiety and Depression Scale (HADS; n=2). The majority of studies measured general depressive symptoms, whilst three studies measured levels of postnatal or antenatal depression (Peltzer & Shikwane, 2011; Brittain et al., 2017; Wong et al., 2017).

Table 1: Characteristics, Measures, Main findings and Quality of Included Studies

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Simbayi et al., (2007), Cape Town	HIV+ adults (n=1063), not reported, 60.5%, African (68%), mixed race/coloured (15%), Indian (12%), white (5%), clinical	C/S	Internalised stigma (adapted AIDS-related stigma scale; Kalichman et al., 2009)	CESD	Stigma: not reported Depression: 30%	Internalised stigma significantly associated with depression (r =0.27, p<0.01). This relationship remained significant after controlling for sociodemographic and health characteristics.	FAIR
Wingood et al., (2008), Rural Western Cape, Province	HIV+ adults (18-45) (n=120), 29 years, 100%, 100% black African, clinical.	C/S	HIV-stigma (HIV-stigma scale; Berger et al., 2001)	CESD	Stigma: not reported Depression: not reported	HIV-stigma associated with depressive symptoms (p=0.003) in univariate analyses. After multivariate analyses, women reporting higher HIV-stigma experienced higher depression (β=0.32, p<0.01).	FAIR
Peltzer & Ramlagan (2011), KwaZulu-Natal	HIV+ adults initiated on ART (n=551), 35.9 years, not reported, not reported, clinical.	PCS (4 months)	Internalised stigma (Internalized AIDS-related stigma scale; Kalichman et al., 2009)	CESD	Stigma: not reported Depression: not reported	Internalised stigma was associated with severe depression (p<0.001), lower CD4 cell counts (p=0.019), discrimination experiences (p=0.001), and lack of social support (p<0.001). In multivariate analyses, CD4 cell counts, QoL, no income, and severe depression (p<0.001) remained as predictors of internalised stigma.	HIGH

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Peltzer & Shikwane (2011), Nkangala district, Mpumalanga	HIV+ adult mothers of infants (n=607), 28.7 years, 100%, 98% black African, clinical.	C/S	Internalised stigma (Internalized AIDS-related stigma scale; Kalichman et al., 2009)	EPDS	Stigma: not reported Depression: 45%	Internalised stigma ($\beta = 1.12, 95\%\ \text{CI}: 1.05 - 1.19, \text{p} < 0.001$) discrimination ($\beta = 1.22, 95\%\ \text{CI}: 1.03 - 1.46$, P=0.023), and social support (β =0.86, 95% CI: 0.74-0.99, p=0.037) associated with depression in both bivariate comparisons and multivariable logistic regression.	HIGH
Pappin et al., (2012), Free State province	HIV+ adults initiated on ART (n=716), 37 years, 75.7%, 98.4% black African, clinical	C/S	HIV-stigma (8-items produced by authors, no additional details reported)	HADS	Stigma: not reported Depression: 25.4%	No univariate results reported. Stigma positively associated with depressive symptoms in multivariate regression analyses (OR=1.13 CI: 1.06-1.20, p<0.01). Participants who attended a support group were less likely to be depressed (OR=0.21, CI: 0.05-0.99, p<0.05).	FAIR

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Breet et al., (2014), several peri-urban townships	HIV+ adults (n=210), 36 years, 40%, 85.2% black African, community.	C/S	HIV-stigma (HIV-stigma scale; Berger et al., 2001)	BDI-II	Stigma: not reported Depression: not reported	Initial regression analyses found HIV-stigma to be a significant predictor of depressive symptoms at stage 1 ($p<0.001$). Social support was also a significant predictor at this stage ($p<0.001$). Relationship between stigma and depression remained with the addition of social support at step 2 ($p<0.01$). Social support was not found to moderate or mediate the relationship between stigma and depression.	LOW

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Wouters et al., (2016), Free State Province	HIV+ adults initiated on ART (n=435), 38.9 years, 77.4%, not reported, clinical	PCS (36 months)	External and internalised stigma (adapted Berger's HIV stigma scale; Wright et al., 2007)	HADS	Stigma: not reported Depression: not reported	No univariate results reported External stigma was positively correlated with depression at wave 1 (β=0.21, p<0.01), whilst internalised stigma was positively correlated at wave 2 (β=0.21, p<0.05), whilst controlling for sociodemographic variables in multivariate analyses. Social support seeking coping was negatively associated with depression at this point (β=-.235, p<0.01).	HIGH
Brittain et al., (2017), Western Cape	HIV+ pregnant women initiating ART (n=623), not reported, 100%, 99.5% black African, clinical.	C/S	Internalised stigma and Social rejection (adapted Social Impact Scale; Fife and Wright, 2000))	EPDS	Stigma: not reported Depression: 11%	Both social rejection (β= 2.2, 95% CI: 1.7-2.7, p<0.001) and internalised shame (β=2.2, 95% CI: 1.8-2.6, p<0.001) were associated with greater depression scores in unadjusted analyses. These relationships remained after multivariate analyses controlling for all covariates [(β=0.7, 95% CI: 0.1-1.3, P<0.001), (β=1.8, 95% CI: 1.2-2.3, p<0.001)]. Internalised presented strongest association. stigma appears to moderate the relationship between social support and depression.	FAIR

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Gamarel et al., (2017), KwaZulu-Natal Province	HIV+ adult parents of HIV- adolescents (n=2477), 44.2 years, 53.9%, 99.8% black African, community.	C/S	Internalised stigma (USAID self-stigma scale, 2006)	CESD	Stigma: not reported Depression: not reported	Parent's internalised stigma was positively correlated with depressive and anxious symptoms (r =0.25, 0.13, p<0.001), as well as child depressive and anxious scores (r=0.12, p<0.001; r=0.16, p<0.001) in univariate analyses. No multivariate analyses conducted.	FAIR
Pantelic et al., (2017), Eastern Cape.	HIV+ adolescents initiated on ART (n=1060), 14 years, 55.2%, not reported, clinical and community.	C/S	Internalised, anticipated and enacted stigma (ALHIV-SS; Pantelic et al., 2016)	CDI	Internalised Stigma: Males 22%, females 25.3% Anticipated Stigma: Males 24.4%, females 34.1% Depression: not reported.	After controlling for age, gender and rural/urban household, internalised HIV-stigma was positively associated with anticipated stigma (β=.28, p<0.001) and depressive symptoms (β=.45, p<0.001). Enacted stigma was also directly associated with depressive symptoms (β=.29, p<0.001).	HIGH

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Wong et al., (2017), Cape Town	HIV+ pregnant adolescent and adult women initiating ART (n=628), 22 (adolescents), 30 (adults), 100%, not reported, clinical	C/S	Internalised shame and Social rejection (Social Impact Scale; Fife & Wright, 2000)	EPDS	Stigma: not reported Depression: 11%	Stigma positively correlated with depressive symptoms in both univariate analyses (β=0.4, 95% CI: 0.3-0.4, P<0.001) and adjusted analyses controlling for sociodemographic variables (β=0.3, 95% CI: 0.3-0.4, p<0.001). Younger age associated with depressive symptoms of depression after controlling for sociodemographic variables and poverty (β=0.9, 95% CI: 0.1-1.8, p=0.04). After stratifying tertiles of stigma, of those with highest levels of stigma, younger women report sig. more depressive symptoms.	FAIR

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Valerie et al., (2018), Soweto.	HIV+ perinatally-infected adolescents (n=250), 16 years, 54.4%, not reported., clinical	C/S	Internalised stigma and associative stigma (Internalized AIDS-Related Stigma Scale; Kalichman et al., 2009).	BDI	Stigma: not reported Depression: 33.8%	Females reported higher internalised stigma scores than males. In bivariate regression analyses, both internalised (β=1.27, 95% CI: 1.19-1.34, p<0.05) and associative (β=1.55, 95% CI: 1.43-1.68, <0.05) stigma were positively correlated with risk of depression. After controlling for sociodemographic variables in multivariate analyses, these relationships remained [(β=1.23 95% CI: 1.13-1.34, p<0.05) and (β=1.59 95% CI: 1.37-1.84, p<0.05), respectively].	FAIR
Casale et al., (2019), Eastern Cape Province	HIV+ adolescents initiated on ART (n=1053), 14 years, 55%, not reported, clinical	C/S	Internalised, anticipated, and enacted stigma (ALHIV-SS; Pantelic et al., 2016).	CDI	Stigma: 43.5% Depression: 46%	Stigma presented significant positive correlation with depression after controlling for covariates (r =0.31, p<0.001). In moderated mediation analyses, greater HIV-stigma directly associated with greater depressive symptoms ($\beta = 0.30, p < 0.001$) as well as suicidal thoughts/behaviour ($\beta = 0.19, p < 0.001$). The latter relationship was mediated by depression. Both forms of support moderated the relationship between stigma and depression.	HIGH

Lead Author (year) & S.A. region	Sample (*n*), mean age, % female, % ethnicity composition, recruitment setting	Study Design	Type of stigma (measure)	Depression measure	Prevalence Findings	Main Stigma X depression findings	Quality assessment
Wadley et al., (2019), Johannesburg	HIV+ adults experiencing chronic pain (n=50), 45 years, 88%, not reported, clinical.	C/S	Perceived stigma (HASI-P; Holzemer et al., 2007)	BDI-II	Stigma: 88% Depression: 24% mild symptoms, 48% moderate-severe symptoms	In univariate analyses, stigma score was positively correlated with intensity of worst pain in the last week (r=0.33, p=0.02) as well as greater depressive symptoms (r=0.33, p=0.02). No multivariate analyses conducted. Mediation analyses did not reveal depression as a mediator of stigma and pain intensity.	FAIR

Abbrevs: C/S = cross sectional, PCS = prospective cohort study, CESD = Centre for Epidemiological Studies Depression Scale, EPDS = Edinburgh Postnatal Depression Scale, HADS = Hospital Anxiety and Depression Scale, BDI = Beck Depression Inventory, BDI-II = Beck Depression Inventory II, CDI = Children's Depression Inventory, CI = Confidence Interval, OR = Odds ratio, HIV+ = HIV-positive.

3.3 *Data Synthesis*

Due to the diversity of study characteristics and measurement tools, a narrative synthesis was conducted as opposed to a meta-analysis (Furlan, Pennick, Bombardier, & van Tulder, 2009). As the majority of included studies were cross-sectional (n=12) causal inference is limited. Meta-analyses are able to measure the consistency of a relationship but are not able to establish causal inferences (Weed, 2010), hence producing a singular effect size may distort findings (Pantelic, Shenderovich, Cluver & Boyes, 2015). As mentioned prior, previous research has demonstrated varying findings across different sub-populations of PLWHA, for example, adolescents (Ashaba et al., 2018), pregnant women (Cuca, Onono, Bukusi & Turan, 2012) and mothers (Turan et al., 2011). Hence, findings from the included studies will be interpreted and compared based upon the HIV-positive sub-population which they include.

3.4 *Quality Assessment*

Results of the quality assessment are available in Table 1. Following appraisal of the cross-sectional studies included in the review (n=12), three were deemed to be of high quality, eight of fair quality, and one of low quality. The features of those judged to be of higher quality included; randomly sampled healthcare facilities and participants, reported high response rates, had higher sample sizes (≥400), involved stigma and depression measures which were validated with the same target population and demonstrated high internal consistency, and employed statistical tests which controlled for relevant confounding variables (e.g., income and CD4 cell counts). Lower quality studies had small sample sizes, low response rates, lacked control of basic confounders (such as age and gender), included measures which were not validated amongst the target population, and did not report or test for the internal consistency of measures.

Both prospective cohort studies were deemed to be of high quality as they included cohorts which were representative of the target population; assessed outcomes based upon medical records or structured interviews; controlled for proven confounding variables (e.g. age, gender, marital status); and exhibited high retention rates.

3.5 *Prevalence of Depression and HIV-stigma*

The following section describes the prevalence rates of HIV-stigma and depression amongst different samples of PLWHA and draws comparison between the different sub-groups included in the studies.

3.5.1 *Stigma Prevalence*

Few studies (n= 3) reported on the prevalence of stigma from their samples. Prevalence rates of stigma within the studies varied depending upon the type of stigma measured. For example, rates of internalised

stigma ranged from 22% to 41%, anticipated stigma scores ranged from 24.4% to 43%, and the prevalence of any stigmatizing experience ranged from 43.5% to 88%. In the studies which sampled adolescents, females were reported to experience significantly higher levels of anticipated stigma than males. Furthermore, participants were more likely to report anticipated than internalised stigma. Higher levels of stigma were reported for adolescents initiated on ART (Casale et al., 2019) in comparison to those not initiated (Pantelic et al., 2017). The highest stigma prevalence was reported by those experiencing comorbid HIV and chronic pain, of whom 88% had experienced some form of stigma. Hence, all studies which reported prevalences within their sample demonstrated high rates of HIV-stigma. Whilst differences emerged across studies the variation could be due to inconsistencies of methodology or sampling. For example, whilst several studies utilised the ALHIV-SS to measure stigma, Casale and colleagues (2019) based their stigma prevalence upon any reported experience of stigma. Hence, it may be difficult to draw comparison between this study and that of Pantelic and colleagues (2017) who drew their prevalence rates from actual cut-off scores. Moreover, of those sampled with comorbid HIV and chronic pain, Wadley, Pincus and Evangeli (2019) produced an intersectional scale combining HIV stigma and chronic-pain stigma measures.

3.5.2 *Depression Prevalence*

Prevalence rates of depression were more commonly reported in the studies than those of stigma (n=8). The prevalence of depression across the studies ranged from between 11% and 48%. Peltzer & Shikwane (2011) found that 45.1% of the mothers in their study were moderately depressed. This high prevalence is consistent with previous research conducted upon similar samples of HIV-positive mothers. For example, Stellenberg and Abrahams (2015) reported that 48.8% of the mothers from a rural South African community scored as ‘moderate’ on their postnatal depression scale. Two studies (Brittain et al., 2017; Wong et al., 2017) measured levels of antenatal depression amongst pregnant women and both reported that 11% of their samples were severely depressed. Furthermore, Brittain and colleagues (2017) reported that an additional 25% of participants were moderately depressed.

In terms of adolescents, Valerie, Earnshaw, Kidman and Violari (2018) and Casale and colleagues (2019) report high rates of depressive symptoms, at 33.8% and 46%, respectively. Other studies have demonstrated mixed scores amongst similar populations. For example, Lwidiko and colleagues (2018) found that 12.9% of Tanzanian HIV-positive adolescents screened positive for depressive symptoms. Interestingly, whilst Casale and colleagues (2019) used the same diagnostic tool, they used a lower cut-off score, and considered the presence of one or more depressive symptoms to be sufficient evidence for diagnosis. Lwidiko and colleagues (2018), contrarily, considered the presence of two coexisting symptoms for a period of two weeks to be an adequate cut-off score, which is consistent with existing research (Ayuso-Mateos et al., 2010). Thus, the aforementioned studies included in this review demonstrate high rates of depressive symptoms amongst adolescents living with HIV. Other studies

have demonstrated differing results and this may be due to disparity of cut-off scores across diagnostic tools, as documented by other researchers (e.g., Wong et al., 2017).

All studies sampling from general adult populations found a high prevalence of depressive symptoms with Pappin, Wouters and Booysen (2012) reporting 25.4%, and Simbayi and colleagues (2007) reporting over a 30% prevalence over the mid-point of cognitive-affective depression scores. Those on ART appeared to demonstrate lower depression scores than those not initiated on ART, which is a consistent finding within the literature (Velloza et al., 2018). Within the study of Wadley, Pincus and Evangeli (2019) 48% of individuals living with comorbid HIV and chronic pain scored moderate to severe on the BDI. Other studies investigating the mental health of HIV-positive individuals experiencing chronic pain and found similar results, for example 36% of the participants in Goodin and colleagues' (2018) study had a psychiatric diagnosis of depression. It is suggested that this high prevalence is due to intersectional health-related stigma faced by those living with HIV *and* chronic pain conditions (Goodin et al., 2018).

In summary, according to the studies which reported a depression prevalence South African pregnant women, mothers, adolescents, and different adult populations are at high risk of experiencing moderate to severe levels of depression. Prevalence rates were higher amongst studies which sampled pregnant women, mothers, and adolescents than studies which sampled from general adult populations (Pappin, Wouters and Booysen, 2012; Simbayi et al., 2007). The highest depression prevalence was reported for those individuals living with comorbid HIV and chronic pain. Variance between these prevalence rates and those of other studies sampling from the sample population may be due to subtle differences in the samples (e.g., socioeconomic status) or differences in the cut-off scores used.

3.6 *Relationships Between HIV-stigma and Depression*

This section describes the association between HIV-stigma and depression amongst different sub-populations of PLHWA in South Africa. All fourteen studies demonstrated a significant positive relationship between HIV-stigma and depression within their samples in univariate analyses. Overall, this relationship was consistent across all measures and forms of stigma (including internalised-, anticipated-, enacted- and overall stigma scores), as well as across studies which sampled from similar sub-populations. Furthermore, the relationships remained significant in multivariate analyses after controlling for basic and complex covariates. Despite the consistency of these findings across studies, there were differences in the HIV-positive sub-population sampled, the measures included, and the covariates tested for. As mentioned previously, certain sub-groups of PLWHA (such as pregnant women, mothers, and adolescents) are at increased risk of experiencing HIV-stigma and depression,

and are often neglected within the literature (e.g., Turan et al., 2011). Hence, the analysis of this section has been split accordingly.

3.6.1 *Adult Populations*

Univariate Analyses

(i) *General Adult Samples:* three studies sampling from general HIV-positive adult populations found significant associations between stigma and depressive symptoms (Simbayi et al., 2007; Wingood et al., 2008; Breet, Kagee & Seedat, 2014). Simbayi and colleagues (2007) found a moderate positive correlation between internalised stigma and depression (r=0.27). Wingood and colleagues (2008), demonstrated a similar relationship within their sample (r=0.33).

(ii) *Adults initiated on ART*: Of the three studies sampling adults initiated on ART, one reported on univariate data (Peltzer & Ramlagan, 2011). Results suggests that internalised stigma has a significant relationship with severe depression (OR: 14.79, 9.13-23.95) and social support (OR: 1.35, 1.121.62). Therefore, those experiencing higher levels of stigma are more likely to experience severe depression, low social support, and are less likely to adhere to ART.

(iii) *Adults Experiencing Chronic Pain:* Wadley, Pincus, and Evangeli, (2019) demonstrated a significant moderate positive correlation between perceived HIV-stigma and depressive symptoms (r=0.33), as well as intensity of pain within the last week (r=0.22). Hence, those with chronic pain who perceive themselves to be stigmatised are more likely to experience depressive symptoms and to report higher levels of pain than those with lower levels of perceived stigma.

Multivariate Analyses

(i) *General Adults Samples*: two studies (Simbayi et al., 2007; Wingood et al., 2008) conducted multivariate analyses on their samples which controlled for sociodemographic variables and length of time since HIV diagnosis. Simbayi and colleagues (2007) additionally controlled for number of HIV symptoms, and found that the relationship between internalised stigma and depression remained significant in multivariate analyses (r=0.20). Wingood and colleagues (2008), similarly, found that amongst their female sample those who reported higher levels of HIV-stigma experienced higher levels of depression (r=0.29).

(ii) *Adults initiated on ART*: all relationships between HIV-stigma and depression remained following multivariate analyses. Each of the three studies sampling adults initiated on ART controlled for sociodemographic characteristics in addition to more complex covariates, such as ART non-adherence,

religious activity, HIV disclosure, rural/urban residence, positive/avoidant coping, drug and alcohol use, condom use, support group attendance, treatment duration, and engagement in peer-adherence intervention. Having controlled for covariates such as these, Wouters, Masquillier and Booysen (2016) found that stigma had the strongest association with depression in their cross-sectional analysis, with wave 1 external stigma being positively associated with depression at wave 1 (β=0.21) and wave 2 internalised stigma being positively associated with wave 2 depression (β=0.21). The authors suggest that these external stigmatizing attitudes and behaviours may become internalised overtime. In prospective analysis, these findings did not hold, as both wave 1 internal and external stigma did not predict depression at wave 2. Despite this, the cross-sectional analysis suggests that those individuals initiated on ART who are currently experiencing higher levels of external and internalised stigma are at greater risk of depression. Interestingly, in their prospective multivariate analyses, Peltzer and Ramlagan (2011) found that severe depression at baseline remained a significant predictor of internalised stigma 12 months later (OR: 5.64, 2.54-12.49). Indeed, those who experienced severe depression were over five times more likely to experience internalised stigma at follow-up. This suggests that the relationship between stigma and depression may be reciprocal, and that depressive symptoms may also influence internalised stigma over time.

Mediation/Moderation

(i) *General Adult Samples*: Breet, Kagee and Seedat (2014) conducted a hierarchical regression in order to determine the role of social support in the relationships between HIV-stigma and depression. The relationship between HIV-stigma and depression remained significant despite social support being added simultaneously in step 2 of the equation. Moreover, the interaction between the two variables was determined to be non-significant. Hence, social support neither mediated nor moderated this relationship.

(ii) *Adults Experiencing Chronic Pain*: having attempted to determine if depression mediates the relationship between HIV-stigma and pain intensity, Wadley, Pincus and Evangeli (2019) found the mediation to be on the threshold of significance. Hence, depression's role in the relationship between stigma and pain intensity remained unclear.

3.6.2 *Mothers and Pregnant Women*

Univariate Analyses

All studies which assessed the relationship between internalised stigma and depressive symptoms (n=3) found a significant positive correlation between the two measures. This indicates that as negative attitudes directed towards the self increased, depressive symptoms tended to increase also. Two studies

assessed the relationship between enacted stigma and depressive symptoms (Peltzer & Shikwane, 2011; Brittain et al., 2017) and both found a significant relationship (OR: 1.28,1.13 - 1.44, p<0.001; OR 2.2, 1.7-2.7, p<0.001). Hence, it is suggested that as experiences of discrimination increase, depression scores also increase. Wong and colleagues (2017), similarly, demonstrated a positive relationship between depressive symptoms and stigma (β=0.3). However internalised and enacted stigma are included as a singular score on the Social Impact Scale and, hence, we cannot draw further comparison between the two forms of stigma. Interestingly, Gamarel, Kuo, Boyes and Cluver (2017) found that the stigma scores of the sampled parents were positively associated with their own depressive symptoms (r=0.25), as well as those of their children (r=0.12). Therefore, those parents which experienced higher levels of HIV-stigma were at greater risk of being depressed as were their HIV-negative children.

Multivariate Analyses

The study conducted by Gamarel, Kuo, Boyes and Cluver (2017) was the only one which did not conduct multivariate analysis. Of those which did, two conducted multivariate linear regression (Brittain et al, 2017; Wong et al., 2017) and one conducted multivariate logistic regression (Peltzer & Shikwane, 2011). The studies identified level of education, time of diagnosis (pre- or post-pregnancy), employment, poverty level, relationship status, accidental or intended pregnancy, age and number of pregnancies as covariates and controlled for them accordingly. After controlling for all sociodemographic characteristics, the relationships between internalised stigma and depression remained statistically significant across all studies. Of those studies which assessed enacted stigma (Brittain et al., 2017; Wong et al., 2017) the relationship between it and depression also remained significant in adjusted analyses. Wong and colleagues (2017) found that after controlling for covariates, younger age (18-24 years) was also associated with greater symptoms of depression. In addition, having stratified tertiles of stigma, of those with the highest levels of stigma, younger women were significantly more likely to experience depressive symptoms than older women. Thus, it is suggested that younger pregnant women who experience high levels of HIV-stigma are more vulnerable to depression than older pregnant women. Furthermore, internalised stigma was reported to present a stronger relationship with depressive symptoms than enacted stigma (β=1.8, p<0.001; β=0.7, p=0.025) (Peltzer & Shikwane, 2011). Having controlled for participant age, age of infant, education level, relationship status and employment status, Peltzer and Shikwane (2011) found that the relationship between internalised stigma, enacted stigma and depression remained significant among mothers of infants.

Social support was included in the multivariate analyses of Brittain and colleagues (2017) and Peltzer and Shikwane (2017) as it has been highlighted as a potentially influential factor in the relationship between HIV-stigma and depression. The relationships between perceived and instrumental social support and depression remained significant in this adjusted model of Brittain and colleagues' (2017) study (perceived emotional, OR: −1.1, −1.6, −0.7; Perceived instrumental, OR: −0.9, −1.3-, −0.4).

Similarly, Peltzer and Shikwane (2011) found that the negative relationship between social support and depressive symptoms remained significant after controlling for covariates (OR: 0.86, 0.74 - 0.99).

Mediation/Moderation

The multivariate analyses demonstrated potential mechanisms for the relationship between HIV-stigma and depression amongst pregnant women and mothers of infants, such as younger age (Wong et al., 2017) and social support (Peltzer & Shikwane, 2011; Brittain et al., 2017). However, only one study (Brittain et al., 2017) examined mediation or moderation effects within their dataset. When stratifying for tertiles of stigma (high, medium, and low), the relationship between social support and depressive symptoms ceased at higher levels of stigma, whilst the relationship between HIV-stigma and depression remained significant at all levels of social support. Hence, the authors suggest that stigma moderates the relationship between social support and depression, but social support does not buffer the effects of stigma.

3.6.3 *Adolescents*

Univariate Analyses

One study conducted univariate analyses (Valerie et al., 2018) and demonstrated significant associations between internalised stigma (OR: 1.27, 1.19-1.34), and associative stigma (OR: 1.55, 1.43-1.68) and levels of depression. Hence, before controlling for covariates, results demonstrate a significant positive relationship between both forms of HIV-stigma and depression.

Multivariate Analyses

All three studies completed multivariate analyses through different statistical means: Pantelic and colleagues (2017) produced a structural equation model consisting of confirmatory factor analysis and pathway models; Valerie, Earnshaw, Kidman and Violari (2018) conducted bivariate Poisson regression analyses; and Casale and colleagues (2019) ran partial correlations. Each study controlled for basic sociodemographic covariates, such as age and gender, as well as more complex covariates. were also controlled for such as rural/urban household location (Pantelic et al., 2017; Casale et al., 2019), food insecurity, orphanhood (Valerie, Earnshaw, Kidman & Violari, 2018), socioeconomic status, mode of HIV infection and whether the primary caregiver is a biological parent (Casale et al., 2019). After controlling for these sociodemographic variables, the relationship between HIV-stigma and depression was found to be statistically significant in each study.

Specifically, having controlled for sociodemographic characteristics, food insecurity, and orphanhood, Valerie and colleagues (2018) reported a positive association between both internalised stigma (OR:

1.23, 1.13-1.34) and associative stigma (OR: 1.59, 1.37-1.84) with depression. Moreover, there was a moderate positive correlation between the two stigma dimensions (r=0.40). Hence, individuals experiencing associative stigma are at greater risk of experiencing internalised stigma (and vice versa), and those experiencing either dimension are at greater risk of depression. Casale and colleagues (2019) also included social support, suicidal thoughts, and suicidal ideation in their multivariate analysis. As a result, they determined HIV-stigma to also possess a significant positive relationship with suicidal thoughts and ideation (r=0.30). Additionally, they reported on a significant negative relationship between perceived social support and depression (r=-0.26), as well as suicidal thoughts and ideation (r=-0.12). Therefore, these results suggest that those adolescents living with HIV who experience higher levels of stigma are more likely to consider taking their own lives. Furthermore, those who consider themselves to receive support from those around them are less inclined to do so and are less likely to be depressed.

Mediation/Moderation

With these findings in mind, Casale and colleagues (2019) conducted a moderated mediation analysis to further explore these relationships. Participation in a HIV support group was found to moderate the positive relationship between HIV-stigma and suicidal thoughts and ideation, whilst depression acted as a mediator. Both support group participation and perceived social support were determined to moderate the relationship between stigma and depression. Hence, only in the presence of both support group participation and perceived social support is the mediated relationship between stigma and suicidal thoughts and suicidal ideation non-significant. These support resources appear to be functioning differently as only support group participation is moderating the relationship between stigma and suicidal thoughts and ideation, whilst perceived social support is the only resource to moderate the direct effect of depression upon suicidal thoughts and ideation.

4. Discussion

This is the first review to systematically assess the relationship between HIV-stigma and depression amongst PLWHA in South Africa. It is also the first review to compare the relationship between these measures across different HIV-positive sub-populations. It included fourteen papers which each represented unique samples from six regions across South Africa. The first aim of this review was to determine the prevalence of HIV-stigma and depression the different sub-populations of PLWHA in South Africa faced and, overall, studies suggested that all sub-populations faced high prevalences of both of these outcomes. The second aim was to assess the association between HIV-stigma and depression amongst these sub-populations and results demonstrated that as levels of HIV-stigma increase, as do levels of depressive symptoms. Adolescents and females experiencing high levels of

stigma appear to be particularly vulnerable to depressive symptoms compared to older adults and males. Also, different associations with depression emerge depending upon the type of stigma measured, with internalised stigma demonstrating a stronger association compared to enacted stigma. Finally, this study aimed to identify potential mediators or moderators of the relationship between HIV-stigma and depression, and studies demonstrated inconsistent findings with regard to the role of social support.

4.1 *Summary of Findings*

Of the fourteen studies included, only eight reported a depression prevalence and three reported HIV-stigma prevalence, and therefore this was under reported. This review found high prevalence rates of HIV-stigma across these studies, ranging from 22% to 43.5%. South African adolescents appear to experience high levels of stigma and females seem particularly vulnerable. More specifically, the only significant gender differences in prevalence were reported for anticipated stigma as females were more likely to experience this form of stigma than males. This finding is consistent with existing research, as a recent systematic review of anticipated HIV-stigma across 31 Sub-Saharan African countries conducted by Chan and Tsai (2016) found that, across over one million study participants, 44% of males reported high levels of anticipated stigma, compared to 53% of females. With regard to different types of stigma, findings suggest that adolescents are more likely to experience anticipated than internalised stigma. This is an interesting finding as the literature examining anticipated stigma amongst HIV-positive populations is sparse, whilst internalised stigma has gained far more attention within research (Golub & Gamarel, 2013). Results also suggest that individuals initiated on ART were more likely to experience some form of HIV-stigma than those not initiated. Finally, adults living with multimorbidites of stigmatised illnesses (e.g. HIV and chronic pain) are at very high risk of experiencing intersectional stigma related to their conditions. Despite these findings, inconsistencies of stigma-prevalence reportage, sampling, and cut-off scores reduces their generalizability and comparability across studies.

Findings also suggested that HIV-positive pregnant women and mothers in the postnatal period are at high risk of depressive symptoms. Differences in depression scores may be attributable to differences between samples, such as engagement in antenatal care or experiences of financial hardship. Depressive symptoms also appear to have a high prevalence with adolescents. However, there is variation of results across studies and this may be due to differences in measurement tools and/or cut-off scores across studies. Finally, studies including general adult samples detect high rates of depression, particularly for those not initiated on ART (Simbayi et al., 2007) and those with comorbid chronic pain (Wadley, Pincus & Evangeli, 2019). In summary, prevalence rates for depression and experiences of stigma are not commonly assessed or reported across the included studies, with no stigma prevalence data reported for mothers or pregnant women. Considering that differences have been documented in terms of stigma

and depression prevalence between different HIV-positive groups, it is key to determine which groups are particularly vulnerable to stigmatizing experiences and which are at highest risk of depression.

In terms of the relationship between HIV-stigma and depression, it is consistently evidenced that there is an association between these two variables amongst different sub-populations of PLWHA in South Africa. Across all of the included studies, every form of stigma which was measured was found to be associated with the study's depression measure and the relationship remained in the studies which conducted multivariate analyses; controlling for sociodemographic variables (e.g., age and gender) and complex covariates (e.g., urban vs. rural residence, CD4 cell count and length of time since diagnosis). Regarding the prospective analyses, Wouters, Masquillier and Booysen (2016) found that, although there was evidence of a cross-sectional association at both time points, neither internal nor external stigma predicted depression over time. Contrarily, Peltzer and Ramlagan (2011) found that severe depression predicted internalised stigma over time, which suggests that the relationship between internalised HIV-stigma and depression may be bidirectional. This finding is in line with the *Integrative Cognitive model of Internalised Stigma* (Wood, Byrne & Morrison, 2017) which suggests that awareness of stigma towards one's 'in-group' stimulates self-abasing beliefs which are bi-directionally associated with emotional and cognitive responses (such as depression) which thereby maintain the self-stigma, and are impacted by protective factors (such as social support).

In terms of pregnant women living with HIV and facing high levels of HIV-stigma, adolescent women (between the ages of 18 and 24) were at greater risk of developing depression than older women (>24 years). This suggests that HIV-positive adolescents experiencing stigma are more vulnerable to depression than adults. This finding may be attributed to features associated with adolescence (such as emotional instability or a lack of coping mechanisms), which may be exacerbated by the stress, stigma and physical symptoms which are synonymous with HIV (Wong et al., 2017). In other words, adolescents may be less equipped to overcome HIV-stigma than adults. Moreover, among pregnant women experiencing HIV-stigma, internalised stigma was a stronger predictor of depression than enacted stigma. This may be due to the "Why try" effect (Corrigan et al., 2015), whereby PLWHA endorse negative attitudes directed towards them, resulting in lower self-esteem, personal motivation, and social contact. Therefore, internalised stigma is associated with additional psychological outcomes in comparison to other forms of stigma, such as enacted stigma.

The role of social support in the relationship between stigma and depression was found to vary across different sub-populations of PLWHA. Contrary to recent evidence from China (Rao et al., 2013), only one of the included studies found social support to mediate the relationship between HIV-stigma and depression. Moreover, depression did not mediate the relationship between HIV-stigma and intensity of pain associated with HIV. Participation in a HIV-support group and high levels of perceived social

support were found to moderate the relationship between HIV-stigma and depression amongst adolescents living with HIV. Finally, stigma moderated the relationship between perceived emotional and instrumental social support and depression amongst pregnant women initiating ART. Existing research conducted upon non-pregnant African-American women has demonstrated that perceived and internalised HIV-stigma mediate the association between support resources and depression (Vyavaharkar et al., 2010). Hence, the role of social support in the relationship between stigma and depression is complex and may vary across different sub-groups of PLWHA. These inconsistent findings could be attributable to the presence of factors which are known to hinder the protective impact of social support in the relationship between HIV-stigma and depression. Countless factors such as, being female (Strebel et al., 2006); being homosexual (Swendeman et al., 2006); and fear of disclosure (Greeff et al., 2008), can impact the buffering effect of social support upon mental health across PLWHA from difference sociodemographic experiences.

4.2. *Implications and Future Research Directions*

A number of studies found different associations between distinct forms of stigma and depression, as well as different relationships between these types of stigma (e.g. internalised and enacted stigma). Hence, as has already been suggested in the literature (Yanos et al., 2015), researchers and policymakers should produce anti-stigma campaigns and interventions which target specific types of stigma, as opposed to combatting stigma generally. Furthermore, particular sub-groups of PLWHA who had experienced stigma were found to be more vulnerable to depression than others. For example, females and adolescents were more likely to be depressed than males or adults. Therefore, policymakers should aim to understand and eradicate any socioeconomic factors which may lead to this disparity, whilst intervention-oriented research should prioritise these 'at-risk' sub-populations.

This review found very few relevant prospective cohort studies and this limits our ability to make causal inferences from the data. Furthermore, despite qualitative studies not being eligible for inclusion in this study, no studies which looked at the relationship between HIV-stigma and depression were excluded for this reason. Hence, there appears to be a dearth of qualitative research investigating this topic. As researchers have long advocated for longitudinal studies (e.g., Pantelic et al., 2015) and studies including qualitative components (e.g., Oskouie et al., 2017) in order to expand the depth of knowledge regarding the effects of HIV-stigma, future studies ought to incorporate these methods.

Whilst all studies clearly demonstrated a relationship between HIV-stigma and depression amongst South African PLWHA, they found differences in the role of social support within this relationship. Moreover, despite evidence demonstrating that social support may play a role in this relationship, only four studies tested for mediation or moderation. As noted by Casale and colleagues (2019), it is unclear

how the direct relationship between stigma and depression is functioning and it is suggested that this indicates the possible existence of additional mediating variables, such as self-esteem (Casale et al., 2013). Furthermore, as social support was only found to play a role in the relationship between HIV-stigma and depression amongst HIV-positive adolescents, it is important that additional efforts are made to investigate why this disparity may arise across sub-populations of PLWHA. Moreover, as prospective analyses reveal a potential bidirectional relationship between internalised stigma and depression (Peltzer & Ramlagan, 2011), future prospective research should aim to more clearly establish this complex association.

Finally, within the included studies (as well as within other research) differences were found in terms of the prevalence of stigma and depression, as well as the relationships between these measures, depending upon gender (e.g., Asiedu & Myers-Bowman, 2014) and age group (e.g., Bekker & Hosek, 2015). Hence, future studies should combat the existing dearth of research which includes and compares both genders, as well as adolescents (e.g., Brandt, 2009; Rueda et al., 2011). In addition, only two studies sampled HIV-positive pregnant women who, as a sub-population, are exposed to a myriad of additional stressors and, hence, are a key demographic for HIV-stigma intervention and mental health research to target in future (Nyamukoho et al., 2019).

4.3 *Strengths and Limitations*

This study possesses several potential limitations. Firstly, despite two of the fourteen studies being prospective cohort studies, the overwhelming majority of studies included conducted cross-sectional analyses in order to assess the relationship between HIV-stigma and depression. As cross-sectional studies measure outcomes at a singular time point, they limit our ability to make causal inferences about HIV-stigma's role in the development of depression amongst PLWHA. Furthermore, as part of the selection criteria, studies were excluded if were not written in English. As English is one of many languages spoken in South Africa (and is the primary language of a mere 10% of the population (South Africa Gateway, 2018)) there is a risk that key articles may have been overlooked. However, prior to language-exclusions, none of the studies which were screened were written in a non-English language. Hence, it is unlikely that language restrictions increased the publication bias of this review. On another note, all included studies identified a significant relationship between HIV-stigma and depression in their samples yet few tested the influence of established correlates of these two outcomes. For example, a mere four studies conducted mediation or moderation analyses on their dataset. Hence, the ability for the studies to make causal inferences is further reduced.

However, this review also demonstrates several notable strengths. Firstly, the study identification process included searches of grey literature databases as well as the reference lists of relevant articles. Failing to do so would have increased the likelihood of overlooking potentially relevant studies. Whilst

the establishment of a global mental health research base has long been advocated by researchers, there exists a disjuncture between the number of peer-reviewed publications produced in HICs and LMICs (Paez, 2017). Hence, grey literature searches are a vital means of limiting publication bias, particularly when the study concerns a LMIC, such as South Africa (Gray, 2013). This is further combatted by the inclusion of a reference-list search which increased the likelihood of detecting articles which may not have been captured by the database search strategy. Furthermore, an additional researcher (AF) was recruited to independently review the search strategy, data extraction template and quality assessment tool. This increases the reliability of the findings by limiting any bias that the primary researcher may have, and reducing the influence this may have upon results. Finally, the studies which were included in this review involved a broad range of different PLWHA populations from South Africa. They represented 9,843 individuals, spanned six regions of South Africa, and sampled from a variety of vulnerable HIV-positive subpopulations; such as pregnant women, adolescents, and individuals initiated on ART. Hence, the results of this review are generalizable to a broad range of PLWHA.

4.4 *Conclusion*

In conclusion, whilst the relationship between HIV-stigma and depression across different sub-populations of PLWHA in South Africa appears to be consistent in cross-sectional analyses, the small number of prospective findings were mixed. Therefore, more longitudinal and mixed-methods research is needed to deepen our understanding of the causal mechanisms underlying the associations between HIV-stigma and depression, including the direction of the relationship. This in order to develop better-informed interventions and public health campaigns which may be used to combat the negative psychological effects of HIV-stigma. Indeed, the role of additional psychosocial variables is still unclear, as findings suggest that the influence of social support appears to differ depending upon the form of stigma being measured and the sub-population sampled. Therefore, future studies should test for mediation and moderation across different psychosocial variables in order to assess how best to protect against the adverse effects of HIV-stigma, and this must be done with specific sub-populations of PLWHA. Furthermore, future research studies must not overlook vulnerable groups such as females and adolescents.

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Appendices

Appendix 1: *Database search terms*

Population	**HIV+ individuals**	HIV/ OR Acquired Immunodeficiency syndrome/ OR AIDS OR AIDS-virus OR acquired immune deficiency syndrome OR acquired immune-deficiency syndrome OR immunologic deficiency syndrome OR human immunodeficiency virus OR HIV infections or HIV seropositivity OR human T-cell leukaemia virus OR HIV-1 OR HIV-2 OR HIV/AIDS
Measure	**HIV-stigma**	Social stigma OR stigma* OR stigma*(adj5 (internali$ed OR self OR public OR structural)) OR HIV-stigma* OR AIDS-stigma* OR HIV-related stigma OR AIDS-related stigma* OR HIV and AIDS-related stigma* OR stereotyping OR prejudice OR social isolation OR social alienation OR social marginalization OR victimi* OR discrimin* OR prejudice* OR stereptyp* OR social exclusion OR shame
Measure	**Depression**	Depression OR depress* OR depressive disorder OR (depress* adj5 (disorder))

Appendix 2: *Example Search Strategy (Ovid Medline)*

1. Exp HIV/
2. Acquired immunodeficiency syndrome/
3. ("AIDS" or "aids virus" or "acquired immune deficiency syndrome" or "acquired immune-deficiency syndrome" or "acquired immunodeficiency syndrome" or "immunologic deficiency syndrome").tw.
4. ("human immunodeficiency virus" or "HIV-infections" or "HIV-seropositivity" or "human T-cell leukaemia virus" or "HIV-1" or "HIV-2").tw.
5. "HIV/AIDS".tw.
6. 1 or 2 or 3 or 4 or 5
7. exp social stigma/
8. stigma*.tw.
9. (stigma* adj5 ("internali$ed" or "self" or "public" or "structural")).tw.
10. ("HIV-stigma*" or "AIDS-stigma*" or "HIV-related stigma*" or "AIDS-related stigma*" or "HIV and AIDS-related stigma*").tw.
11. (stigma adj5 ("HIV" or "AIDS" or "HIV/AIDS")).tw.
12. stereotyping/ or prejudice/ or social isolation/ or social alienation/ or social marginalization/
13. ("victimi*" or "discrimin" or "prejudice*" or "shame" or "stereotyp*" or "social exclusion").tw.
14. 7 or 8 or 9 or 10 or 11 or 12 or 13
15. Depression/
16. Depress*.tw.
17. Exp depressive disorder/
18. 15 or 16 or 17
19. 6 and 14 and 18

Appendix 3: *Data Extraction Table*

Title:	
Authors:	
Journal: AIDS and Behaviour	**Year**:
Aims:	
Study Design:	

Sample:

N:	**Mean age**:	**Sample**:	**Gender (%)**:
Other demographic variables?		**Region in South Africa:**	
		Number of Controls:	
Inclusion criteria:			
Exclusion criteria:			
Recruitment method:			

Measures:

HIV-Stigma		
What aspect of HIV-stigma was measured?		
Instrument:		
(1) Self-administered or (2) Experimenter Administered:		
No of items:	**Measure valid/reliable?** **Cultural relevance:**	**Cronbach's a?**
Depression:		
What was measured:		
Instrument:		
(1) Self-administered or (2) Experimenter Administered:		
No of items:	**Measure valid/reliable?**	**Cronbach's a?**
Other Measures:		

Other psychological factors measured/controlled for?

Results:

Main findings (type of relationship & evidence):
Is there any evidence of a relationship? ( ) Yes / ( ) No
Does the relationship remain when other variables are controlled for?
Mediation/Moderation tested?
Author's Interpretations:
Author's Limitations:
Reviewers' Limitations:

Other comments:

Quality assessment score:

Appendix 4: *Quality assessment tools*

(i) Adapted Cambridge Quality Checklist (CQC) for quality assessment of primary studies. Adapted with reference to adaptation conducted by Pantelic et al., 2015.

Facility Sampling
3 total population or random sampling
2 Purposive Sampling
1 Convenience Sampling
0 Not reported

Within-Facility Sampling
3 total population or random sampling
2 Purposive Sampling
1 Convenience Sampling
0 Not reported

Response Rates
2 Response or retention rates (for longitudinal) (greater than or equal to 70%) or differential attrition (less than or equal to 10%)
1 response or retention rate less than 70% or differential attrition >10%
0 Not reported

Sample Size
1 greater than or equal to 400
0 less than or equal to 400

Stigma Measure(s) validity
3 Use of a validated standardized scale with the same target population OR use of an adapted scale that had been validated with another target population
2 Validation of a newly developed instrument
1 Use of a non-validated measurement
0 Not reported

Stigma Measure(s) reliability
2 Reliability coefficient greater than or equal to 0.7
1 Reliability coefficient less than 0.7
0 Not reported

Depression Measure Validity
3 Use of a validated standardized scale with the same target population OR use of an adapted scale that had been validated with another target population
2 Validation of a newly developed instrument
1 Use of a non-validated measurement
0 Not reported

Depression Measure(s) reliability
2 Reliability coefficient greater than or equal to .7
1 reliability coefficient less than .7
0 Not reported

Study Design Score

3 Prospective cohort data used in analysis (longitudinal)
2 retrospective data e.g. case-control
1 cross-sectional data used in analysis

Confounding Variables

(Analysis – correlations only or multivariate including confounding variables)

2 Accounts for basic and additional confounding variables, more complex analysis

1 Multivariate analysis accounting for basic confounding variables either during recruitment or analysis. E.g. age, gender.

0 No attempt to control for confounding factors in recruitment or analyses, correlations only.

*Grading system: overall CQC score is determined by calculating a percentage for each study based on the point-score they achieve out of a potential 24 points. Studies were low quality if their CQC score was between 0% and 33%; fair quality if they were between 34% and 66%; and high if they were between 67% and 100%.

(ii) *Newcastle-Ottawa Quality Assessment Form for Cohort Studies* (Wells et al., 2008).

Newcastle-Ottawa Quality Assessment Form for Cohort Studies

Note: A study can be given a maximum of one star for each numbered item within the Selection and Outcome categories. A maximum of two stars can be given for Comparability.

Selection

1) Representativeness of the exposed cohort
   a) Truly representative ***(one star)***
   b) Somewhat representative ***(one star)***
   c) Selected group
   d) No description of the derivation of the cohort
2) Selection of the non-exposed cohort
   a) Drawn from the same community as the exposed cohort ***(one star)***
   b) Drawn from a different source
   c) No description of the derivation of the non exposed cohort
3) Ascertainment of exposure
   a) Secure record (e.g., surgical record) ***(one star)***
   b) Structured interview ***(one star)***
   c) Written self report
   d) No description
   e) Other
4) Demonstration that outcome of interest was not present at start of study
   a) Yes ***(one star)***
   b) No

Comparability

1) Comparability of cohorts on the basis of the design or analysis controlled for confounders
   a) The study controls for age, sex and marital status ***(one star)***
   b) Study controls for other factors (list) _____ ***(one star)***
   c) Cohorts are not comparable on the basis of the design or analysis controlled for confounders

Outcome

1) Assessment of outcome
   a) Independent blind assessment ***(one star)***
   b) Record linkage ***(one star)***
   c) Self report
   d) No description
   e) Other
2) Was follow-up long enough for outcomes to occur
   a) Yes ***(one star)***
   b) No

Indicate the median duration of follow-up and a brief rationale for the assessment above:_____

3) Adequacy of follow-up of cohorts
   a) Complete follow up- all subject accounted for ***(one star)***
   b) Subjects lost to follow up unlikely to introduce bias- number lost less than or equal to 20% or description of those lost suggested no different from those followed. ***(one star)***
   c) Follow up rate less than 80% and no description of those lost
   d) No statement

Thresholds for converting the Newcastle-Ottawa scales to AHRQ standards (good, fair, and poor):

Good quality: 3 or 4 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Fair quality: 2 stars in selection domain AND 1 or 2 stars in comparability domain AND 2 or 3 stars in outcome/exposure domain

Poor quality: 0 or 1 star in selection domain OR 0 stars in comparability domain OR 0 or 1 stars in outcome/exposure domain

Appendix 5: *Author publication instructions for target journal*

Target Journal: *AIDS and Behaviour*

AIDS and Behaviour instructions for authors may be retrieved through the following link:

https://www.springer.com/public+health/journal/10461?print_view=true&detailsPage=pltci_649262

Appendix 6: *Research Project Outline*

Project Title: *The Relationship between HIV/AIDS-related stigma and Depression in Adolescents living in Sub-Saharan Africa*

Supervisor: Karen Wetherall

Student ID: XXXXXXX

Justification:

Mental health research has mainly centred around high-income countries, yet the HIV pandemic has re-centred LMICs and placed less developed countries towards the forefront in terms of research need (Saxena et al., 2007). The World Health Organization have reported that 36.9 million people are currently living with HIV across the globe (WHO, 2018). Of these individuals, around 70% reside in Africa (UNAIDS, 2017). Yet, the current evidence base regarding the psychological effects of HIV diagnosis is imbalanced toward high-income countries (Collins et al., 2006). Whilst rates of infection have steadily decreased the world over, amongst adolescents the number of new infection has been gradually increasing – thus forming around half of new diagnoses in 2003 (CDCP, 2004). People living with HIV (PLWH) are not only likely to experience a myriad of physical side effects, but are also extremely vulnerable to mental health issues, particularly depression which affects between 15% and 60% of PLWH (Ayano, Solomon & Abraha, 2018). Those experiencing HIV and depression are less likely to adhere to antiretroviral therapy (Waldrop-Valverde & Valverde, 2005), to have lower CD4 cell counts, and worse disease progression (Ironson et al., 2005). Recent research has attributed this increased likelihood of depression to experiences of stigma (Rao et al., 2007). Negative effects of HIV-stigma upon the mental health of PLWH have been widely reported in both high-, low- and middle-income countries (Mburu et al., 2014).

Despite this, very little research has been conducted upon HIV+ adolescents in Africa and, indeed, those with comorbid depression (Collins et al., 2006). Qualitative research has been extremely important in considering the psychosocial factors that impact PLHIV. Qualitative research has indicated, more clearly, the impact of HIV-stigma upon health and well-being, as well as ability to access health and social care services (e.g. Chambers et al., 2015). For example, several studies have indicated cases of discrimination involving confidentiality breaches and humiliation at the hands of healthcare workers (Chambers et al., 2015). Other studies have demonstrated the detrimental impact of this upon an individual's self-concept (Fife & Wright, 2000). Qualitative studies have demonstrated, more clearly, individual manifestations and experiences of stigma in healthcare and how this may impact wellbeing. Chambers and colleagues (2015) produced a qualitative synthesis

which demonstrates specific facets of the stigmatizing experience of HIV status. Difficulty coping with misperceptions, social separation, denigration, and discriminatory actions associated with their diagnosis were highlighted as poignant features of HIV-stigma and the mechanisms through which it impacts individuals' lives. Qualitative studies have been particularly useful in the development of interventions to combat the effects of HIV-stigma. However, as noted by Pulerwitz and colleagues (2010), for example, the development of accurate interventions has been halted by a lack of reliable quantitative evidence lacking comparative measures and data across studies. Hence, this is an important area of study.

In a review involving studies from all across Africa, Brandt (2009, p. 124) included very few studies including measures of HIV-related stigma and, furthermore, studies were excluded if they included non-adult participants. Breuer and colleagues (2011) investigated the relationship between HIV/AIDS and mental health in sub-Saharan Africa. However, stigma was superficially investigated and depression was included as one of many mental health outcomes. Moreover, they did not include information regarding the age of the samples. Lowther and colleagues (2014) included a majority of studies from LMICs (n=34/66) but only assessed prevalence rates, and a lot of included studies lacked demographic information, therefore it is difficult to distinguish between subgroups. Rueda and colleagues (2016) explicitly examined the relationship between HIV-related stigma and health outcomes. However, they did not include information regarding age demographics of participants, and only included depression superficially. Moreover, they included 64 studies, but only 14 were conducted in LMICs, and six were conducted in African countries.

Aims: (1) to determine whether a relationship exists between HIV-stigma and depression and what this is and (2) to compare adolescents to other sub-populations of PLWHA.

Literature Search:
Two reviewers (author and AM) shall independently search PROSPERO and Cochrane Central Register of Controlled Trials using the keywords 'HIV' and 'stigma OR victimi* OR discrimi*', to avoid substantial similarity with other reviews. The reviewers shall then search the following electronic databases to identify potentially relevant studies, as well as the reference lists of articles: MEDLINE, PsycINFO, CINAHL and Web of Science. If any disagreement shall arise in terms of study selection, a third reviewer shall be consulted to determine inclusion/exclusion.

The databases will be searched using the following terms: depress* AND (HIV OR AIDS OR acquired immunodeficiency syndrome OR human immunodeficiency virus) AND (stigma* OR discrimi* OR vicimi*).

The study population shall be limited to African countries. The reference sections of articles shall be hand-searched for further references. Grey literature websites shall be searched (OpenGrey and OAIster) in order to decrease publication bias.

Inclusion/exclusion criteria:

Inclusion:

- Published in English
- Participants with depression (either through clinical diagnosis or cut-off score on a self-report scale).
- Participants from African countries.
- Quantitative studies.
- Studies assessing levels of HIV/AIDS-stigma.
- Participants with and form of HIV/AIDS (e.g., perinatal, postnatal etc.).
- Studies including data specifically regarding adolescents.
- Studies which measure relationship between stigma and depression.

Exclusion:

- Qualitative studies
- Studies which exclude/have no data regarding adolescents
- Participants without comorbid HIV/AIDS and depression.
- Studies which do not include participants from Africa
- Studies which do not quantitatively assess levels of HIV/AIDS stigma.

Timetable:

1. Identify relevant studies – by the end of February
2. Search studies for inclusion/exclusion criteria – beginning of march
3. Write introduction/methods – end of march
4. Data extraction – April
5. Analyse data and interpret results – may/june

**Author's Note:* Whilst the original research project aimed to understand the relationship between HIV-stigma and depression amongst adolescents, database results revealed too few results to conduct a systematic review. Hence, studies including any age group were searched for. Having done so, too many results (39) were generated which is beyond the scope of a master's thesis. Therefore, studies were limited to those conducted in South Africa.

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