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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004200
Article Type:	Research
Date Submitted by the Author:	08-Oct-2013
Complete List of Authors:	Spies, Georgina; Stellenbosch University, Psychiatry Seedat, Soraya; Stellenbosch University, Psychiatry
Primary Subject Heading:	Mental health
Secondary Subject Heading:	HIV/AIDS
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Depression & mood disorders < PSYCHIATRY

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DEPRESSION AND RESILIENCE IN HIV-INFECTED WOMEN WITH EARLY LIFE STRESS: DOES TRAUMA PLAY A MEDIATING ROLE?

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Keywords: HIV/AIDS, Depression, trauma, resilience, mediation

Word count: 3204

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ABSTRACT

Objectives: The present study sought to assess the relationship between depressive symptomatology and resilience among HIV-infected women and to investigate whether trauma exposure (childhood trauma, other discrete lifetime traumatic events) or the presence of posttraumatic stress symptomatology mediated this relationship.

Design: Cross-sectional study.

Setting: Western Cape, South Africa.

Participants: A convenience sample of 95 HIV-infected women in peri-urban communities in the Western Cape, South Africa. All the women had exposure to moderate to severe childhood trauma as determined by the Childhood Trauma Questionnaire.

Primary and secondary outcome measures: We examined the relationship between depressive symptomatology and resilience and investigated whether trauma exposure or the presence of posttraumatic stress symptomatology mediated this relationship through the Sobel test for mediation and PLS path analysis.

Results: There was a significant negative correlation between depressive symptomatology and resilience ($p = < .01$). PLS path analysis revealed a significant direct effect between depression and resilience. On the Sobel test for mediation, distal (childhood trauma) and proximal traumatic events did not significantly mediate this association ($p = > .05$). However, posttraumatic stress symptomatology significantly mediated the relationship between depression and resilience in trauma exposed women living with HIV.

Conclusions: In the present study, higher levels of resilience resulted in lower levels of self-reported depression. Although causal inferences are not possible, this suggests that in this sample, resilience may act as protective factor against the development of clinical

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depression. The results also indicate that posttraumatic stress symptoms (PTSS), which are highly prevalent in HIV-infected and trauma exposed individuals and often comorbid with depression, may further explain and account for this relationship. Further investigation is required to determine if early identification and treatment of PTSS in this population may ameliorate the onset and persistence of major depression.

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ARTICLE SUMMARY

Strengths and limitations of this study

- This is the first study investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals and to find evidence of a mediating effect of posttraumatic symptoms on this relationship
- Potential recall bias on the retrospective rating scales may influence the findings.
- The cross-sectional study design precludes causal inferences and longitudinal assessment of this relationship is necessary.

BACKGROUND

In South Africa, an estimated 5.63 million individuals are infected with human immunodeficiency virus (HIV). Of these, 3.3 million are females [1]. High rates of intimate partner violence (IPV), rape, and childhood abuse have been reported [2-4]. Studies suggest high rates of childhood emotional (51.9%), physical (51.1%), and sexual (41.6%) abuse in HIV-positive individuals [5]. HIV has become a manageable chronic disease with the increased use of highly active antiretroviral therapies (HAART). However, this chronicity is

coupled with an increase in the number of lifetime emotional and physical challenges faced by infected individuals [6]. Common mental disorders such as depression and anxiety are highly prevalent and comorbid with HIV/AIDS. Compared to the general population and comparable HIV-negative individuals, evidence suggests that the prevalence of depression is two to four fold higher in HIV-infected individuals [7-10]. Prevalence rates of depression in HIV-positive individuals range from 5% to 20% across a majority of studies [11]. In South African studies, high rates of depression and posttraumatic stress disorder (PTSD) have been reported among HIV-infected individuals [12-16]. The most commonly reported psychiatric disorders among HIV-positive individuals with a history of childhood maltreatment include substance abuse, major depressive disorder, and posttraumatic stress disorder [17]. Research shows that childhood abuse and exposure to other traumas are among the risk factors for the development of adult psychopathology [18-22]. However, not every individual who experiences early life stress or other traumatic incidents will develop a psychiatric disorder, highlighting the importance of resilience [23, 24]. Human responses to stress and trauma differ widely. Some individuals develop psychiatric disorders, such as PTSD and depression; others develop psychological symptoms that resolve rapidly, while others report no symptoms in response to traumatic stress [25]. Numerous risk and protective factors, including developmental, cognitive, psychological (e.g. personality traits, coping style, social support) genetic, epigenetic and neurobiological (neurochemistry and neural circuitry) mechanisms, have been shown to play a role in how individuals respond to stress and trauma [25, 26]. Resilience is a multidimensional construct and is understood as an individual's ability to bounce back from hardship and trauma [25]. Resilience refers to a person's ability to adapt successfully to acute stress, trauma or more chronic forms of adversity [24]. Resilience represents the personal qualities that enable one to thrive in the

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face of adversity [27]. Resilience may be viewed as a measure of stress coping ability and, as such, could be an important target of treatment in anxiety, depression, and stress reactions [27]. However, there is relatively little awareness about resilience and its relationship to these disorders. In non-HIV samples, traumatic experiences such as childhood maltreatment and adult life stress, have been reported, among depressed patients, to influence treatment response [28, 29]. In patients with PTSD, high resilience has been associated with favourable treatment outcomes [30]. Recent data also indicates that in depressed patients resilience contributes to more favourable treatment outcomes with the effects of resilience even more definitive when combined with low trait anxiety [31].

To our knowledge, there are no studies investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals. In light of this, the present study sought to examine this relationship in a sample of trauma exposed HIV-infected women.

METHODS

Participants

The study cohort consisted of 95 HIV-positive women who were enrolled in a larger prospective cognitive and imaging study. All the women had exposure to childhood trauma as defined on the Childhood Trauma Questionnaire (CTQ). Eligibility criteria included: willingness and ability to provide written informed consent, ability to read and write in either English or Afrikaans at 5th grade level, aged between 18 and 65 years, medically well enough to undergo neuropsychological testing and MRI scanning. Exclusions included: a current or past history of schizophrenia, bipolar disorder or other psychotic disorders, current substance or alcohol abuse or dependence, significant previous head injury,

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demonstrated frank dementia on the International HIV Dementia Scale, current seizure disorders of any cause, history of CNS infections of neoplasms, hepatitis B positive status, and current use or use within the last month of any psychotropic medication.

Procedure

The study was approved by the ethics committee of Stellenbosch University, South Africa. All participants were recruited by a researcher or with the help of doctors and adherence counselors from community health care facilities in and around the Cape Town area. All participants who consented were screened for eligibility and childhood trauma exposure either in person at their clinic or telephonically. Those who met initial screening criteria subsequently underwent behavioural, neuromedical, neurocognitive and neuroimaging assessments at Stellenbosch University. Participants were reimbursed for their travel costs to the University on two separate occasions.

Measures

Demographic and clinical characteristics

Age, gender, marital status, ethnicity, years of education and employment status were captured. A comprehensive history was obtained from, and a general physical examination conducted in, all patients. Virologic markers of disease progression (CD4 lymphocyte count and viral loads) were obtained from blood samples.

Psychiatric morbidity

Current and lifetime psychiatric disorders were evaluated using the MINI- International Neuropsychiatric Interview- Plus (M.I.N.I.-Plus) [32].

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Depression

Participants were assessed for depressive symptomatology using the Center for Epidemiologic Studies Depression Scale (CES-D) [33]. The CES-D is a 20-item widely used self-report instrument designed to measure depressive symptomatology. The scale was specifically designed to measure depressive symptomatology in the general population, unlike previous depression scales which have been predominantly used in clinical populations. The CES-D emphasises the affective component of depressive symptomatology, namely depressed mood. Each item comprises a likert scale ranging from 0 to 3. A total score for the 20 items is obtained, with the lowest possible score being 0 and the highest possible score being 60. Higher scores are indicative of more severe depression.

Traumatic life events

Exposure to traumatic life events were assessed for using the Life Events Checklist (LEC) [34]. The LEC is a widely used measure of exposure to potentially traumatic events. It was developed in order to facilitate the diagnosis of posttraumatic stress disorder (PTSD). One of the LEC's unique features is that it enquires about various types of exposure to each potentially traumatic event. Therefore, the LEC elicits whether the participant experienced, witnessed, or learned of the traumatic event, a feature that other traumatic event measures do not possess. Participants rate their experience of each traumatic event listed on a likert scale. A total score is derived from the sum of experiencing and/or witnessing the event. Higher scores are indicative of the experience of more traumatic life events.

Posttraumatic stress symptomatology

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Posttraumatic stress symptomatology was assessed using the Davidson Trauma Scale (DTS) [35]. The DTS is a widely used 17-item self-report and measures symptoms of PTSD on frequency and severity scales. The items are categorised according to the criteria set out in the DSM-IV: criteria B (intrusive re-experiencing) criteria C (avoidance and numbness) and criteria D (hyperarousal). For each item, the participant rates the frequency and severity during the previous week on 5-point (0 to 4) scales, with the lowest possible score being 0 and the highest possible score being 136. Higher scores are indicative of more PTSD symptoms.

Childhood trauma

The Childhood Trauma Questionnaire Short Form (CTQ-SF) [36], a 28-item self-report inventory that provides valid screening for histories of abuse and neglect was administered. It assesses five types of maltreatment including, emotional, physical, and sexual abuse, and emotional and physical neglect. These five subscales each consist of 5 items with scores ranging from 5 to 25. The overall trauma score ranges from 25 to 125 with higher scores indicating higher levels of childhood trauma (score of 25-31 = no trauma, score of 41-51 = low to moderate, 56-68 = moderate to severe, and 73-125 = severe to extreme).

Resilience

Resilience was assessed using the Connor Davidson Resilience Scale (CD-RISC) [27, 35]. The CD-RISC is a self-report measure of resilience consisting of 25 items. The scale rates participants over the past month with a total score of the CD-RISC varying from 0-100. The items are scored on a 5 point likert scale, with higher scores reflecting higher resilience.

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Data Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 and Statistica, version 11.0.

Basic statistical analyses were conducted, which included descriptive statistics. Spearman correlation and multiple linear regression analyses were carried out to assess the relationship between the variables of interest.

According to Baron and Kenny (1986), a variable functions as a mediator when it meets the following conditions: (1) variations in the levels of the independent variable (IV) significantly account for variations in the mediator variable (MV) [figure 1, path *a*], (2) variations in the MV significantly account for variations in the dependent variable (DV) [figure 1, path *b*], and (3) when paths *a* and *b* are controlled for, a previous significant relation between the IV and DV is no longer significant, with the strongest demonstration of mediation occurring when path *c* (figure 1) is zero [37]. Rather than hypothesising a direct causal relationship between the IV and DV, a mediational model hypothesises that that IV influences the MV, which in turn influences the DV. In order to assess for a mediation effect, several steps were taken. Firstly, the Sobel test for mediation was conducted to assess whether childhood trauma, traumatic life events, or posttraumatic stress symptoms mediated the relationship between the dependent (depression) and independent variables (resilience). Secondly, to test for mediation, one should conduct three regression equations. Separate coefficients for each equation should be estimated and tested [37]. First, the MV should be regressed on the IV; second, the DV should be regressed on the IV; and third, the DV should be regressed on both the IV and the MV [37]. To establish mediation, the following conditions should be met: First, the IV must affect the MV in the first equation; second, the IV must be shown to

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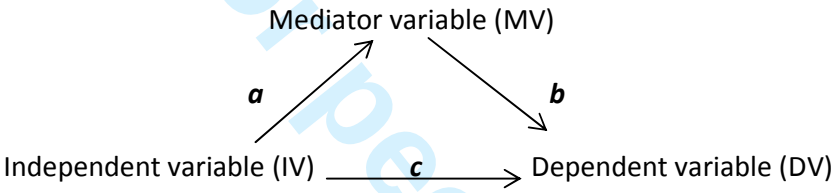
affect the DV in the second equation; and third, the MV must affect the DV in the third equation. The effect of the IV on the DV should be less in the third equation than in the second. If the IV has no effect when the MV is controlled, then this is indicative of perfect mediation [37]. Lastly, a PLS path analysis was performed to confirm the results of the aforementioned analyses.

Figure 1. Mediation model



RESULTS

Demographic characteristics of the sample

Participants were predominantly black (98.9%), Xhosa (African indigenous language) speaking (93.7%) women, with a mean age of 33.6 years (range 21-50). The mean highest level of education was 9.98 years, ranging from 5 to 14 years. The majority were single (73.7%), unemployed (70.5%), and reported a combined annual household income of less than $1,000 (10 000 ZAR) per year (87.4%).

Clinical characteristics of the sample

The mean CD4 lymphocyte count was 438.40 cells/mm^3 (range 25-1529 cells/mm^3). The mean HIV viral load was 106,157.05 copies/ml, ranging from below the detectable limit to 3,200,000 copies/ml. The lower limit for detection was 40 copies/ml. The predominant

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HIV clade was subtype C. Forty four (46%) of the women were on antiretroviral treatment (ARTs).

Depression, PTSD and resilience scores

The mean score on the CES-D was 17.7, with a minimum of 0 and a maximum of 60. The mean score on the DTS was 25.5, with a minimum of 0 and a maximum of 116. A total of 7 women (6.5%) met criteria for current MDD and 9 (8.4%) for recurrent MDD on the MINI-Plus. Two women (1.9%) met criteria for PTSD on the MINI-Plus. The mean score on the CD-RISC was 81.7 with a minimum of 24 and a maximum of 100, respectively.

Trauma exposure

All women reported experiencing childhood trauma. The mean score on the CTQ was in the moderate to severe range (65.5), with a minimum of 41 and a maximum of 114. However, these women were also exposed to other discrete traumas regarded as index events for the development of PTSD. The commonest traumatic life events reported included: physical assault, transport accident, fire/explosion, life-threatening illness or injury and the sudden unexpected death of a loved one. Table 1 lists all the index traumas reported in this cohort of women.

Table 1. List of traumatic life events experienced (n = 95).

Index trauma (experienced or witnessed)	*Sum (n)*	*Percentage (%)*
Natural disaster	15	15.8
Fire/explosion	50	52.7
Transport accident	59	62.1
Serious accident at work, home or while doing sports	23	24.2
Physical assault	69	72.6

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Assaulted with a weapon	52	54.7
Sexual assault	35	36.8
Other unwanted/uncomfortable sexual experience	17	17.9
Exposure in a war zone	8	8.5
Captivity (kidnapped, abducted, held hostage)	9	9.5
A life-threatening illness or injury	47	49.5
Exposure to sudden/violent death (murder, suicide)	24	25.3
Sudden or unexpected death of someone close	43	45.2
Serious injury, harm or death you caused to someone else	12	12.7
Badly beaten by parents or guardian as a child	23	24.2
Badly beaten by a spouse or partner	34	35.8
Other life-threatening experience not listed	8	8.5

Reliability analysis

Cronbach alpha coefficients for all measures ranged from good to excellent: CTQ (α = .73), LEC (α = .78), DTS (α = .89), CD-RISC (α = .94), CES-D (α = .96).

Correlation between variable of interest

Pearson's correlation coefficients were calculated to assess the relationship between all the variables of interest. There was a significant negative correlation between depression (CES-D) and resilience (CD-RISC) scores, r = -0.28, p = < 0.01. In addition, there was a significant negative correlation between posttraumatic stress symptoms (DTS) and resilience (CD-RISC), r = -0.23, p = < 0.05. These correlations suggest that higher levels of resilience resulted in lower levels of self-reported depression and posttraumatic stress symptoms. Moreover, Pearson's correlation coefficients were calculated to assess the relationship between the IV and MV, and the MV and DV. The IV and DV were significantly correlated with two of the presumed MVs, namely childhood trauma (CTQ) and posttraumatic stress symptoms (DTS).

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However, traumatic life events (LEC) were not significantly correlated with either the IV or DV, suggesting that this variable is not a mediator (Table 2).

Table 2. Pearson's correlation coefficients for all variables of interest (n = 95).

Variable 1	Variable 2	Pearson r	p value
CTQ	CESD	0.23	0.02
CTQ	LEC	0.12	0.27
CTQ	DTS	-0.01	0.94
CTQ	CDRS	0.22	0.04
CESD	LEC	0.15	0.15
CESD	DTS	0.48	<0.01
CESD	CDRS	-0.28	<0.01
LEC	DTS	0.18	0.08
LEC	CDRS	-0.02	0.84
DTS	CDRS	-0.23	0.03

CDRS = Connor Davidson Resilience Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DTS = Davidson Trauma Scale; CTQ = Childhood Trauma Scale; LE = Life Events Checklist.

Multiple linear regression

Multiple linear regression with depression (CES-D score) as the outcome variable revealed a significant model of 4 factors: childhood trauma (β =.330, p = .002), other trauma exposure (β = .181, p = .718), posttraumatic stress symptomatology (β =.216, p = .000), and resilience (β = -.236, p = .007), of which 3 of the 4 variables were significantly associated with depression (Table 3). This model explains 35% of the variance of depressive symptomatology (R^2= 0.35). As expected, childhood trauma and posttraumatic stress symptoms contributed to depression severity while resilience appeared to reduce it.

Table 3. Regression model for depressive symptomatology (CES-D score) (n = 95).

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Variable	*df*	β	SE of β	*p*	R^2	Adjusted R^2
Model	4	-	-	.000	.347	.318
Childhood trauma (CTQ)	1	.330	.101	.002		
Other trauma (LEC)	1	.181	.499	.718		
Trauma symptoms (DTS)	1	.216	.045	.000		
Resilience (CD-RISC)	1	-.236	.085	.007		

Sobel test for mediation

To assess for mediation, the Sobel test for mediation was performed. The results showed that neither childhood trauma (CTQ) nor stressful life events (LEC) significantly mediated the relationship between depression and resilience in this sample ($p > 0.05$). However, the results demonstrated that posttraumatic stress symptomatology (DTS) was a significant mediator ($p < 0.05$).

Regression analysis

To confirm whether posttraumatic stress symptomatology (MV) in fact mediated the relationship between depression (DV) and resilience (IV), three separate regression equations were conducted following the guidelines described in the data analysis section. The first regression equation showed that the IV significantly influenced the MV, p = .027. The second regression equation showed that the IV significantly influenced the DV, p = .005. The third regression equation showed that the MV significantly influenced the DV, p = .000. The effect of the IV on the DV was less in the third equation than in the second equation, p = .005 vs. p = .049. This is indicative of partial mediation. Posttraumatic stress symptoms

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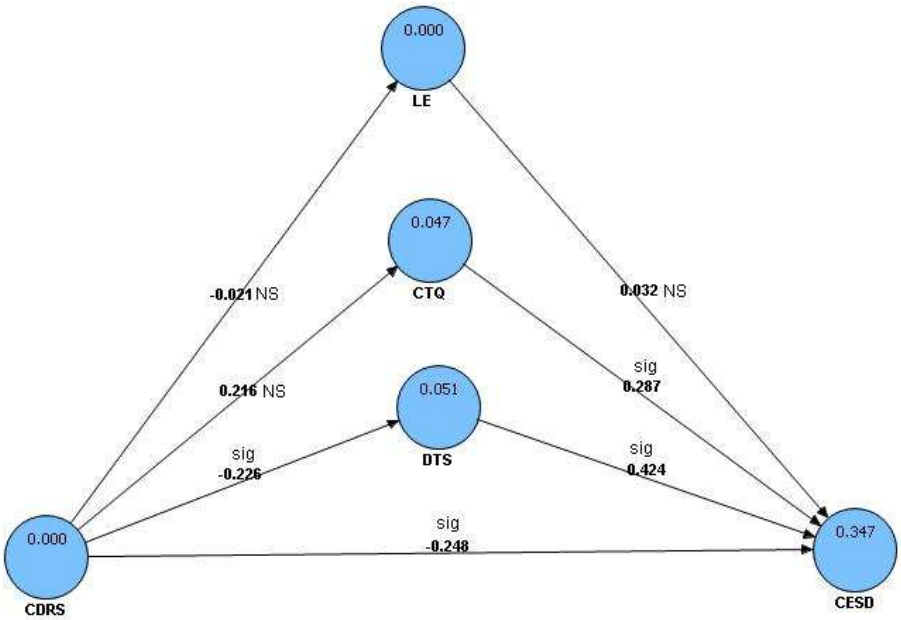
accounts for some, but not all, of the relationship between depression and resilience. Partial mediation implies that there is not only a significant relationship between the mediator and the dependent variable, but also some direct relationship between the independent and dependent variable.

PLS path analysis

The PLS path analysis revealed a significant direct effect between depression and resilience ($p < .05$). The PLS path analysis also revealed that the effects via DTS (posttraumatic stress symptoms) were also significant ($p < .05$). This implies that although there is a mediating effect, there is also evidence of a direct effect. The other presumed mediators (CTQ and LEC) were not significant ($p > .05$). See figure 2.

Figure 2. PLS path analysis for all variables of interest.



CDRS = Connor Davidson Resilience Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DTS = Davidson Trauma Scale; CTQ = Childhood Trauma Scale; LE = Life Events Checklist.

DISCUSSION

In this cross-sectional study of 95 HIV-infected women, we found that childhood trauma, posttraumatic stress symptoms and resilience independently predicted depressive symptoms. Childhood trauma and posttraumatic stress symptomatology contributed to depression, while resilience appeared to mitigate it. The results demonstrated a significant association between depression and resilience in this cohort, with resilience acting as a protective buffer. Posttraumatic stress symptoms were found to mediate this relationship and accounted for some, but not all, of the relationship between depression and resilience.

A cut-off score of 16 or greater on the CES-D has been used to identify individuals at risk for clinical depression. Although, the mean score on the CES-D for this cohort was 17.7, this score is still relatively low. Results revealed a significant negative association between depression and resilience in this cohort of women, suggesting that resilience may be acting as a protective buffer against the development of clinically significant depression. The mean score on the CD-RISC was 81.7, suggesting high levels of resilience.

Childhood trauma and posttraumatic stress symptoms independently predicted depressive symptoms but other traumatic life events did not. Mediation analyses demonstrated that childhood trauma did not mediate the relationship between depression and resilience but posttraumatic stress symptoms did. This suggests that it is not the experience of trauma itself that contributes to depression per se, but the psychological manifestation thereof, in this case posttraumatic stress symptoms. A score of 40 and greater has been used to identify individuals with clinically significant PTSD. The mean score on the DTS in this cohort was substantially lower (25.5), once again highlighting the possible role of resilience in this cohort of women. This mediational model suggests that in this cohort, resilience influences

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(reduces) posttraumatic stress symptoms, which in turn influences (reduces) depressive symptoms. However, this is a partial mediation, suggesting that there is also evidence of a direct link between depression and resilience. Resilience appears to act as a protective buffer against depression, irrespective of the mediating role of posttraumatic stress symptoms.

The finding that childhood trauma and posttraumatic stress symptoms were each associated with depression is in keeping with other studies. Given that these women all reported early life stress and a number of other traumatic life events, this finding was expected. HIV-infected individuals are at risk for psychiatric disorders such as depression and PTSD [12-16]. In the South African context, PTSD is not an uncommon disorder in individuals with HIV/AIDS. In some cases, PTSD is secondary to the diagnosis of HIV/AIDS but in most cases it is seen after other traumas [15]. In addition, evidence suggests that major depressive disorder is more likely to be associated with PTSD in HIV infected individuals [15].

Prior studies have examined effects of resilience on adult psychopathology [20, 23] and depressive symptom severity [38] in individuals with childhood abuse and/or other trauma exposure. However, this is the first study, to our knowledge, to explore the relationship between resilience and depression in a cohort of HIV-infected women with childhood trauma and to find evidence of a mediating effect of posttraumatic symptoms on this relationship. In light of the study findings, it is important to screen not only for depression but also for comorbid posttraumatic stress symptoms in HIV-infected individuals and to develop interventions that enhance resilience among these individuals.

The results of the present study should be interpreted in light of the study limitations, including potential recall bias on the retrospective rating scales, the cross-sectional study

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design and the potential confounding effect of comorbid psychiatric disorders. Future studies with longitudinal assessment of this hypothesis are needed. Understanding how resilience can be enhanced is of great importance to not only promoting coping mechanisms but also alleviating maladaptive coping and stress responses in common mental illnesses such as depression and PTSD [26].

Acknowledgements

We would like to acknowledge Professor Martin Kidd for providing statistical assistance.

Contributors

SS made substantial contributions to the conception and design, analysis of data, revising the manuscript and providing final approval of the version to be published. GS made a substantial contribution to conception and design, acquisition of data, analysis and interpretation of data, drafting and revising the article and providing final approval of the version to be published. All authors listed on the manuscript met all ICMJE criteria for authorship.

Funding

This work is supported by the South African Research Chair in PTSD hosted by Stellenbosch University, funded by the DST and administered by NRF, the Claude Leon Foundation and the South African Medical Research Council.

Competing interests

We declare we have no competing interests.

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REFERENCES

1 UNAIDS. Worlwide HIV & AIDS statistics. http://www.avert.org/worldstats.htm. Accessed September 09, 2013.

2 Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: relevance for HIV prevention in hyperendemic countries of southern Africa. *AIDS* 2008;**22**:73-86.

3 Jewkes R, Penn-Kekana L, Levin J, Ratsaka M, Schrieber M. Prevalence of emotional, physical and sexual abuse of women in three South African provinces. *S Afr Med J* 2001; **91**:421-428.

4 Kalichman SC, Simbayi LC. Sexual assault history and risks for sexually transmitted infections among women in an African township in Cape Town, South Africa. *AIDS Care* 2004;**16**:681-689.

5 Wilson HW, Widom CS. An examination of risky sexual behavior and HIV in victims of child abuse and neglect: a 30-year follow-up. *Health Psychol* 2008;**27**:149-158.

6 Crepaz N, Passin WF, Herbst JH, Rama SM, Malow RM, Purcell DW, et al. Meta-analysis of cognitive-behavioral interventions on HIV-positive persons' mental health and immune functioning. *Health Psychol* 2008;**27**:4-14.

7 Bing EG, Burnam MA, Longshore D, Fleishman JA, Sherbourne CD, London AS, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Arch Gen Psychiatry* 2001;**58**:721-728.

8 Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 2001;**158**:725-730.

For peer review only

9 Morrison MF, Petitto JM, Ten Have T, Gettes DR, Chiappini MS, Weber AL, et al. Depressive and anxiety disorders in women with HIV infection. *Am J Psychiatry* 2002; **159**:789-796.

10 Rabkin JG, Johnson J, Lin SH, Lipsitz JD, Remien RH, Williams JB, et al. Psychopathology in male and female HIV-positive and negative injecting drug users: longitudinal course over 3 years. *AIDS* 1997;**11**:507-515.

11 Cruess DG, Evans DL, Repetto MJ, Gettes D, Douglas SD, Petitto JM. Prevalence, diagnosis, and pharmacological treatment of mood disorders in HIV disease. *Biol Psychiatry* 2003;**54**:307-316.

12 Myer L, Smit J, Roux LL, Parker S, Stein DJ, Seedat S. Common Mental Disorders among HIV-Infected Individuals in South Africa: Prevalence, Predictors, and Validation of Brief Psychiatric Rating Scales. *AIDS Patient Care & STDs* 2008;**22**:147-158.

13 Olley BO, Gxamza F, Seedat S, Theron H, Taljaard J, Reid E, et al. Psychopathology and coping in recently diagnosed HIV. *S Afr Med J* 2003;**93**:928-931.

14 Olley BO, Seedat S, Nei DG, Stein DJ. Predictors of Major Depression in Recently Diagnosed Patients with HIV/AIDS in South Africa. *AIDS Patient Care & STDs* 2004;**18**:481-487.

15 Olley BO, Zeier MD, Seedat S, Stein DJ. Post-traumatic stress disorder among recently diagnosed patients with HIV/AIDS in South Africa. *AIDS Care* 2005;**17**:550-557.

16 Olley BO, Seedat S, Stein DJ. Persistence of psychiatric disorders in a cohort of HIV/AIDS patients in South Africa: A 6-month follow-up study. *J Psychosom Res* 2006;**61**:479-484.

For peer review only

17 Spies G, Afifi TO, Archibald SL, Fennema-Notestine C, Sareen J, Seedat S. Mental health outcomes in HIV and childhood maltreatment: a systematic review. *Syst Rev* 2012;**1**:1-30.

18 Alim TN, Graves E, Mellman TA, Aigbogun N, Gray E, Lawson W, et al. Trauma exposure, posttraumatic stress disorder and depression in an African-American primary care population. *J Natl Med Assoc* 2006;**98**:1630-1636.

19 Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. *Depress Anxiety* 1999;**9**:169-174.

20 Collishaw S, Pickles A, Messer J, Rutter M, Shearer C, Maughan B. Resilience to adult psychopathology following childhood maltreatment: evidence from a community sample. *Child Abuse Negl* 2007;**31**:211-229.

21 Lizardi H, Klein DN, Ouimette PC, Riso LP, Anderson RL, Donaldson SK. Reports of the childhood home environment in early-onset dysthymia and episodic major depression. J *Abnorm Psychol* 1995;**104**:132-139.

22 Ritchie K, Jaussent I, Stewart R, Dupuy AM, Courtet P, Ancelin ML, et al. Association of adverse childhood environment and 5-HTTLPR Genotype with late-life depression. *J Clin Psychiatry* 2009;**70**:1281-1288.

23 Alim TN, Feder A, Graves RE, Wang Y, Weaver J, Westphal M, et al. Trauma, resilience, and recovery in a high-risk African-American population. *Am J Psychiatry* 2008;**165**:1566-1575.

24 Feder A, Nestler EJ, Charney DS. Psychobiology and molecular genetics of resilience. *Nat Rev Neurosci* 2009;**10**:446-457.

For peer review only

25 Southwick SM, Charney DS. The science of resilience: implications for the prevention and treatment of depression. *Science* 2012;**338**:79-82.

26 Wu G, Feder A, Cohen H, Kim JJ, Calderon S, Charney DS, et al. Understanding resilience. *Front Behav Neurosci* 2013;**7**:10-25.

27 Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety* 2003;**18**:76-82.

28 Enns MW, Cox BJ. Psychosocial and clinical predictors of symptom persistence vs remission in major depressive disorder. *Can J Psychiatry* 2005;**50**:769-777.

29 Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *Am J Psychiatry* 2012; **169**:141-151.

30 Davidson JR, Payne VM, Connor KM, Foa EB, Rothbaum BO, Hertzberg MA, et al. Trauma, resilience and saliostasis: effects of treatment in post-traumatic stress disorder. *Int Clin Psychopharmacol* 2005;**20**:43-48.

31 Min JA, Lee NB, Lee CU, Lee C, Chae JH. Low trait anxiety, high resilience, and their interaction as possible predictors for treatment response in patients with depression. *J Affect Disord* 2012;**137**:61-69.

32 Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;**59**:22-33.

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33 Radloff SF. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement* 1977;**1**:385-401.

34 Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric Properties of the Life Events Checklist. *Assessment* 2004;**11**:330-341.

35 Davidson JRT, Book SW, Colket JT, Tupler LA, Roth S, David D, et al. Assessment of a new self-rating scale for post-traumatic stress disorder. *Psychol Med* 1997;**27**:153-160.

36 Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl* 2003;**27**:169-190.

37 Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**:1173-1182.

38 Wingo AP, Wrenn G, Pelletier T, Gutman AR, Bradley B, Ressler KJ. Moderating effects of resilience on depression in individuals with a history of childhood abuse or trauma exposure. *J Affect Disord* 2010;**126**:411-414.

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DEPRESSION AND RESILIENCE IN HIV-INFECTED WOMEN WITH EARLY LIFE STRESS: DOES TRAUMA PLAY A MEDIATING ROLE? A CROSS-SECTIONAL STUDY.

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2013-004200.R1
Article Type:	Research
Date Submitted by the Author:	22-Jan-2014
Complete List of Authors:	Spies, Georgina; Stellenbosch University, Psychiatry Seedat, Soraya; Stellenbosch University, Psychiatry
Primary Subject Heading:	Mental health
Secondary Subject Heading:	HIV/AIDS
Keywords:	HIV & AIDS < INFECTIOUS DISEASES, PSYCHIATRY, Anxiety disorders < PSYCHIATRY, Depression & mood disorders < PSYCHIATRY

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DEPRESSION AND RESILIENCE IN HIV-INFECTED WOMEN WITH EARLY LIFE STRESS: DOES TRAUMA PLAY A MEDIATING ROLE? A CROSS-SECTIONAL STUDY.

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Keywords: HIV/AIDS, Depression, trauma, resilience, mediation

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ABSTRACT

Objectives: The present study sought to assess the relationship between depressive symptomatology and resilience among HIV-infected women and to investigate whether trauma exposure (childhood trauma, other discrete lifetime traumatic events) or the presence of posttraumatic stress symptomatology mediated this relationship.

Design: Cross-sectional study.

Setting: Western Cape, South Africa.

Participants: A convenience sample of 95 HIV-infected women in peri-urban communities in the Western Cape, South Africa. All the women had exposure to moderate to severe childhood trauma as determined by the Childhood Trauma Questionnaire.

Primary and secondary outcome measures: We examined the relationship between depressive symptomatology and resilience (the Connor-Davidson Resilience Scale) and investigated whether trauma exposure or the presence of posttraumatic stress symptomatology mediated this relationship through the Sobel test for mediation and PLS path analysis.

Results: There was a significant negative correlation between depressive symptomatology and resilience (p = < .01). PLS path analysis revealed a significant direct effect between depression and resilience. On the Sobel test for mediation, distal (childhood trauma) and proximal traumatic events did not significantly mediate this association (p = > .05). However, posttraumatic stress symptomatology significantly mediated the relationship between depression and resilience in trauma exposed women living with HIV.

Conclusions: In the present study, higher levels of resilience were associated with lower levels of self-reported depression. Although causal inferences are not possible, this suggests

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that in this sample, resilience may act as protective factor against the development of clinical depression. The results also indicate that posttraumatic stress symptoms (PTSS), which are highly prevalent in HIV-infected and trauma exposed individuals and often comorbid with depression, may further explain and account for this relationship. Further investigation is required to determine if early identification and treatment of PTSS in this population may ameliorate the onset and persistence of major depression.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is the first study investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals and to find evidence of a mediating effect of posttraumatic symptoms on this relationship
- Potential recall bias on the retrospective rating scales may influence the findings.
- The cross-sectional study design precludes causal inferences and longitudinal assessment of this relationship is necessary.

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BACKGROUND

In South Africa, an estimated 5.63 million individuals are infected with human immunodeficiency virus (HIV). Of these, 3.3 million are females [1]. High rates of intimate partner violence (IPV), rape, and childhood abuse have been reported [2-4]. Studies suggest high rates of childhood emotional (51.9%), physical (51.1%), and sexual (41.6%) abuse in HIV-positive individuals [5]. HIV has become a manageable chronic disease with the increased use of highly active antiretroviral therapies (HAART). However, this chronicity is coupled with an increase in the number of lifetime emotional and physical challenges faced by infected individuals [6]. Common mental disorders such as depression and anxiety are highly prevalent and comorbid with HIV/AIDS. Compared to the general population and comparable HIV-negative individuals, evidence suggests that the prevalence of depression is two to four fold higher in HIV-infected individuals [7-10]. Prevalence rates of depression in HIV-positive individuals range from 5% to 20% across a majority of studies [11]. In South African studies, high rates of depression and posttraumatic stress disorder (PTSD) have been reported among HIV-infected individuals [12-16]. The most commonly reported psychiatric disorders among HIV-positive individuals with a history of childhood maltreatment include substance abuse, major depressive disorder, and posttraumatic stress disorder [17]. Research shows that childhood abuse and exposure to other traumas are among the risk factors for the development of adult psychopathology [18-22]. However, not every individual who experiences early life stress or other traumatic incidents will develop a psychiatric disorder, highlighting the importance of resilience [23, 24]. Human responses to stress and trauma differ widely. Some individuals develop psychiatric disorders, such as PTSD and depression; others develop psychological symptoms that resolve rapidly, while others report no symptoms in response to traumatic stress [25]. Numerous risk and

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protective factors, including developmental, cognitive, psychological (e.g. personality traits, coping style, social support) genetic, epigenetic and neurobiological (neurochemistry and neural circuitry) mechanisms, have been shown to play a role in how individuals respond to stress and trauma [25, 26]. Resilience is a multidimensional construct and is understood as an individual's ability to bounce back from hardship and trauma [25]. Resilience refers to a person's ability to adapt successfully to acute stress, trauma or more chronic forms of adversity [24]. Resilience represents the personal qualities that enable one to thrive in the face of adversity [27]. Resilience may be viewed as a measure of stress coping ability and, as such, could be an important target of treatment in anxiety, depression, and stress reactions [27]. However, there is relatively little awareness about resilience and its relationship to these disorders. In non-HIV samples, traumatic experiences such as childhood maltreatment and adult life stress, have been reported, among depressed patients, to influence treatment response [28, 29]. In patients with PTSD, high resilience has been associated with favourable treatment outcomes [30]. Recent data also indicates that in depressed patients resilience contributes to more favourable treatment outcomes with the effects of resilience even more definitive when combined with low trait anxiety [31].

To our knowledge, there are no studies investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals. In light of this, the present study sought to examine this relationship in a sample of trauma exposed HIV-infected women.

METHODS

Participants

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A total of 230 HIV-infected and uninfected women, with and without trauma exposure consented to participate and were enrolled into a larger prospective cognitive and imaging study. Of these, 95 HIV-positive women had exposure to childhood trauma as defined on the Childhood Trauma Questionnaire (CTQ) and were included in the present study. A score of 41 and higher on the CTQ was used as the cut-off for exposure to childhood trauma. Eligibility criteria included: willingness and ability to provide written informed consent, ability to read and write in either English or Afrikaans at 5th grade level, aged between 18 and 65 years, medically well enough to undergo neuropsychological testing and MRI scanning. Exclusions included: a current or past history of schizophrenia, bipolar disorder or other psychotic disorders, current substance or alcohol abuse or dependence, significant previous head injury, demonstrated frank dementia on the International HIV Dementia Scale, current seizure disorders of any cause, history of CNS infections of neoplasms, hepatitis B positive status, and current use or use within the last month of any psychotropic medication.

Procedure

The study was approved by the ethics committee of Stellenbosch University, South Africa. All participants were recruited by a researcher or with the help of doctors and adherence counselors from community health care facilities in and around the Cape Town area. All participants who consented were screened for eligibility and childhood trauma exposure either in person at their clinic or telephonically. Those who met initial screening criteria subsequently underwent behavioural, neuromedical, neurocognitive and neuroimaging assessments at Stellenbosch University. Participants were reimbursed for their travel costs to the University on two separate occasions.

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Measures

Demographic and clinical characteristics

Age, gender, marital status, ethnicity, years of education and employment status were captured. A comprehensive history was obtained from, and a general physical examination conducted in, all patients. Virologic markers of disease progression (CD4 lymphocyte count and viral loads) were obtained from blood samples.

Psychiatric morbidity

Current and lifetime psychiatric disorders were evaluated using the MINI- International Neuropsychiatric Interview- Plus (M.I.N.I.-Plus) [32].

Depression

Participants were assessed for depressive symptomatology using the Center for Epidemiologic Studies Depression Scale (CES-D) [33]. The CES-D is a 20-item widely used self-report instrument designed to measure depressive symptomatology. The scale was specifically designed to measure depressive symptomatology in the general population, unlike previous depression scales which have been predominantly used in clinical populations. The CES-D emphasises the affective component of depressive symptomatology, namely depressed mood. Each item comprises a likert scale ranging from 0 to 3. A total score for the 20 items is obtained, with the lowest possible score being 0 and the highest possible score being 60. Higher scores are indicative of more severe depression.

Traumatic life events

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Exposure to traumatic life events were assessed for using the Life Events Checklist (LEC) [34]. The LEC is a widely used measure of exposure to potentially traumatic events. It was developed in order to facilitate the diagnosis of posttraumatic stress disorder (PTSD). One of the LEC's unique features is that it enquires about various types of exposure to each potentially traumatic event. Therefore, the LEC elicits whether the participant experienced, witnessed, or learned of the traumatic event, a feature that other traumatic event measures do not possess. Participants rate their experience of each traumatic event listed on a likert scale. A total score is derived from the sum of experiencing and/or witnessing the event. Higher scores are indicative of the experience of more traumatic life events.

Posttraumatic stress symptomatology

Posttraumatic stress symptomatology was assessed using the Davidson Trauma Scale (DTS) [35]. The DTS is a widely used 17-item self-report and measures symptoms of PTSD on frequency and severity scales. The items are categorised according to the criteria set out in the DSM-IV: criteria B (intrusive re-experiencing) criteria C (avoidance and numbness) and criteria D (hyperarousal). For each item, the participant rates the frequency and severity during the previous week on 5-point (0 to 4) scales, with the lowest possible score being 0 and the highest possible score being 136. Higher scores are indicative of more PTSD symptoms.

Childhood trauma

The Childhood Trauma Questionnaire Short Form (CTQ-SF) [36], a 28-item self-report inventory that provides valid screening for histories of abuse and neglect was administered. It assesses five types of maltreatment including, emotional, physical, and sexual abuse, and

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emotional and physical neglect. These five subscales each consist of 5 items with scores ranging from 5 to 25. The overall trauma score ranges from 25 to 125 with higher scores indicating higher levels of childhood trauma (score of 25-31 = no trauma, score of 41-51 = low to moderate, 56-68 = moderate to severe, and 73-125 = severe to extreme).

Resilience

Resilience was assessed using the Connor Davidson Resilience Scale (CD-RISC) [27, 35]. The CD-RISC is a self-report measure of resilience consisting of 25 items. The content of the scale reflects hardiness, control, commitment, personal or collective goals, change or stress viewed as a challenge/opportunity, strengthening effect of stress, past successes, recognition of limits to control, engaging the support of others, self-efficacy, optimism, action orientation, self-esteem/confidence, adaptability, tolerance of negative affect, problem solving skills, humour in the face of stress, patience, faith and secure bonds to others. Examples of items include: “I am able to adapt when changes occur”, “I have at least one close and secure relationship which helps me when I am stressed”, “when there are no clear solutions to my problems, sometimes fate or God can help”, “under pressure I stay focused and think clearly”, “I try to see the humorous side of things when I am faced with problems.” The scale rates participants over the past month with a total score of the CD-RISC varying from 0-100. The items are scored on a 5 point likert scale, with higher scores reflecting higher resilience.

Data Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 and Statistica, version 11.0.

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Basic statistical analyses were conducted, which included descriptive statistics. Spearman correlation and multiple linear regression analyses were carried out to assess the relationship between the variables of interest.

According to Baron and Kenny (1986), a variable functions as a mediator when it meets the following conditions: (1) variations in the levels of the independent variable (IV) significantly account for variations in the mediator variable (MV) [figure 1, path *a*], (2) variations in the MV significantly account for variations in the dependent variable (DV) [figure 1, path *b*], and (3) when paths *a* and *b* are controlled for, a previous significant relation between the IV and DV is no longer significant, with the strongest demonstration of mediation occurring when path *c* (figure 1) is zero [37]. Rather than hypothesising a direct causal relationship between the IV and DV, a mediational model hypothesises that that IV influences the MV, which in turn influences the DV. In order to assess for a mediation effect, several steps were taken. Firstly, the Sobel test for mediation was conducted to assess whether childhood trauma, traumatic life events, or posttraumatic stress symptoms mediated the relationship between the dependent (depression) and independent variables (resilience). Secondly, to test for mediation, one should conduct three regression equations. Separate coefficients for each equation should be estimated and tested [37]. First, the MV should be regressed on the IV; second, the DV should be regressed on the IV; and third, the DV should be regressed on both the IV and the MV [37]. To establish mediation, the following conditions should be met: First, the IV must affect the MV in the first equation; second, the IV must be shown to affect the DV in the second equation; and third, the MV must affect the DV in the third equation. The effect of the IV on the DV should be less in the third equation than in the second. If the IV has no effect when the MV is controlled, then this is indicative of perfect

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mediation [37]. Lastly, a PLS path analysis was performed to confirm the results of the aforementioned analyses.

RESULTS

Demographic characteristics of the sample

Participants were predominantly black (98.9%), Xhosa (African indigenous language) speaking (93.7%) women, with a mean age of 33.6 years (range 21-50). The mean highest level of education was 9.98 years, ranging from 5 to 14 years. The majority were single (73.7%), unemployed (70.5%), and reported a combined annual household income of less than $1,000 (10 000 ZAR) per year (87.4%).

Clinical characteristics of the sample

The mean CD4 lymphocyte count was 438.40 cells/mm^3 (range 25-1529 cells/mm^3). The mean HIV viral load was 106,157.05 copies/ml, ranging from below the detectable limit to 3,200,000 copies/ml. The lower limit for detection was 40 copies/ml. The predominant HIV clade was subtype C. Forty four (46%) of the women were on antiretroviral treatment (ARTs).

Depression, PTSD and resilience scores

The mean score on the CES-D was 17.7, with a minimum of 0 and a maximum of 60. The mean score on the DTS was 25.5, with a minimum of 0 and a maximum of 116. A total of 7 women (6.5%) met criteria for current MDD and 9 (8.4%) for recurrent MDD on the MINI-Plus. Two women (1.9%) met criteria for PTSD on the MINI-Plus. The mean score on the CD-RISC was 81.7 with a minimum of 24 and a maximum of 100, respectively.

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Trauma exposure

All women reported experiencing childhood trauma. The mean score on the CTQ was in the moderate to severe range (65.5), with a minimum of 41 and a maximum of 114. However, these women were also exposed to other discrete traumas regarded as index events for the development of PTSD. The commonest traumatic life events reported included: physical assault, transport accident, fire/explosion, life-threatening illness or injury and the sudden unexpected death of a loved one. Table 1 lists all the index traumas reported in this cohort of women.

Table 1. List of traumatic life events experienced (n = 95).

Index trauma (experienced or witnessed)	*Sum (n)*	*Percentage (%)*
Natural disaster	15	15.8
Fire/explosion	50	52.7
Transport accident	59	62.1
Serious accident at work, home or while doing sports	23	24.2
Physical assault	69	72.6
Assaulted with a weapon	52	54.7
Sexual assault	35	36.8
Other unwanted/uncomfortable sexual experience	17	17.9
Exposure in a war zone	8	8.5
Captivity (kidnapped, abducted, held hostage)	9	9.5
A life-threatening illness or injury	47	49.5
Exposure to sudden/violent death (murder, suicide)	24	25.3
Sudden or unexpected death of someone close	43	45.2
Serious injury, harm or death you caused to someone else	12	12.7
Badly beaten by parents or guardian as a child	23	24.2
Badly beaten by a spouse or partner	34	35.8

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Other life-threatening experience not listed	8	8.5

Internal consistency

Cronbach alpha coefficients for all measures ranged from good to excellent: CTQ (α = .73), LEC (α = .78), DTS (α = .89), CD-RISC (α = .94), CES-D (α = .96).

Correlation between variable of interest

Pearson's correlation coefficients were calculated to assess the relationship between all the variables of interest. There was a significant negative correlation between depression (CES-D) and resilience (CD-RISC) scores, r = -0.28, p = < 0.01. In addition, there was a significant negative correlation between posttraumatic stress symptoms (DTS) and resilience (CD-RISC), r = -0.23, p = < 0.05. These correlations suggest that higher levels of resilience resulted in lower levels of self-reported depression and posttraumatic stress symptoms. Moreover, Pearson's correlation coefficients were calculated to assess the relationship between the IV and MV, and the MV and DV. The IV and DV were significantly correlated with two of the presumed MVs, namely childhood trauma (CTQ) and posttraumatic stress symptoms (DTS). However, traumatic life events (LEC) were not significantly correlated with either the IV or DV, suggesting that this variable is not a mediator (Table 2).

Table 2. Pearson's correlation coefficients for all variables of interest (n = 95).

Variable 1	Variable 2	Pearson r	p value
CTQ	CESD	0.23	0.02
CTQ	LEC	0.12	0.27
CTQ	DTS	-0.01	0.94

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CTQ	CDRS	0.22	0.04
CESD	LEC	0.15	0.15
CESD	DTS	0.48	<0.01
CESD	CDRS	-0.28	<0.01
LEC	DTS	0.18	0.08
LEC	CDRS	-0.02	0.84
DTS	CDRS	-0.23	0.03

CDRS = Connor Davidson Resilience Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DTS = Davidson Trauma Scale; CTQ = Childhood Trauma Scale; LE = Life Events Checklist.

Multiple linear regression

Multiple linear regression with depression (CES-D score) as the outcome variable revealed a significant model of 4 factors: childhood trauma (β =.330, p = .002), other trauma exposure (β = .181, p = .718), posttraumatic stress symptomatology (β =.216, p = .000), and resilience (β = -.236, p = .007), of which 3 of the 4 variables were significantly associated with depression (Table 3). This model explains 35% of the variance of depressive symptomatology (R^2= 0.35). As expected, childhood trauma and posttraumatic stress symptoms contributed to depression severity while resilience appeared to reduce it.

Table 3. Regression model for depressive symptomatology (CES-D score) (n = 95).

Variable	*df*	β	SE of β	*p*	R^2	Adjusted R^2
Model	4	-	-	.000	.347	.318
Childhood trauma (CTQ)	1	.330	.101	.002		
Other trauma (LEC)	1	.181	.499	.718		
Trauma symptoms (DTS)	1	.216	.045	.000		
Resilience (CD-RISC)	1	-.236	.085	.007		

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Sobel test for mediation

To assess for mediation, the Sobel test for mediation was performed. The results showed that neither childhood trauma [CTQ] ($z = 1.77$, $p = 0.08$) nor stressful life events [LEC] ($z = -0.19$, $p = 0.84$) significantly mediated the relationship between depression and resilience in this sample. However, the results demonstrated that posttraumatic stress symptomatology (DTS) was a significant mediator ($z = -2.03$, $p = 0.04$).

Regression analysis

To confirm whether posttraumatic stress symptomatology (MV) in fact mediated the relationship between depression (DV) and resilience (IV), three separate regression equations were conducted following the guidelines described in the data analysis section. The first regression equation showed that the IV significantly influenced the MV, ($\beta = -.226$, $p = .027$). The second regression equation showed that the IV significantly influenced the DV, ($\beta = -.283$, $p = .005$). The third regression equation showed that the MV significantly influenced the DV, ($\beta = .442$, $p = .000$). The effect of the IV on the DV was less in the third equation than in the second equation, $\beta = -.183$ ($p = .049$) vs. $\beta = -.283$ ($p = .005$). This is indicative of partial mediation. Posttraumatic stress symptoms accounts for some, but not all, of the relationship between depression and resilience. Partial mediation implies that there is not only a significant relationship between the mediator and the dependent variable, but also some direct relationship between the independent and dependent variable.

PLS path analysis

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The PLS path analysis revealed a significant direct effect between depression and resilience ($p < .05$). The PLS path analysis also revealed that the effects via DTS (posttraumatic stress symptoms) were also significant ($p < .05$). This implies that although there is a mediating effect, there is also evidence of a direct effect. The other presumed mediators (CTQ and LEC) were not significant ($p > .05$). See figure 2.

DISCUSSION

In this cross-sectional study of 95 HIV-infected women, we found that childhood trauma, posttraumatic stress symptoms and resilience independently predicted depressive symptoms. Childhood trauma and posttraumatic stress symptomatology contributed to depression, while resilience appeared to mitigate it. The results demonstrated a significant association between depression and resilience in this cohort, with resilience acting as a protective buffer. Posttraumatic stress symptoms were found to mediate this relationship and accounted for some, but not all, of the relationship between depression and resilience.

A cut-off score of 16 or greater on the CES-D has been used to identify individuals at risk for clinical depression. Although, the mean score on the CES-D for this cohort was 17.7, this score is still relatively low. Results revealed a significant negative association between depression and resilience in this cohort of women, suggesting that resilience may be acting as a protective buffer against the development of clinically significant depression. The mean score on the CD-RISC was 81.7, suggesting high levels of resilience.

Childhood trauma and posttraumatic stress symptoms independently predicted depressive symptoms but other traumatic life events did not. Mediation analyses demonstrated that childhood trauma did not mediate the relationship between depression and resilience but posttraumatic stress symptoms did. This suggests that it is not the experience of trauma

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itself that contributes to depression per se, but the psychological manifestation thereof, in this case posttraumatic stress symptoms. A score of 40 and greater has been used to identify individuals with clinically significant PTSD. The mean score on the DTS in this cohort was substantially lower (25.5), once again highlighting the possible role of resilience in this cohort of women. This mediational model suggests that in this cohort, resilience influences (reduces) posttraumatic stress symptoms, which in turn influences (reduces) depressive symptoms. However, this is a partial mediation, suggesting that there is also evidence of a direct link between depression and resilience. Resilience appears to act as a protective buffer against depression, irrespective of the mediating role of posttraumatic stress symptoms.

The finding that childhood trauma and posttraumatic stress symptoms were each associated with depression is in keeping with other studies. Given that these women all reported early life stress and a number of other traumatic life events, this finding was expected. HIV-infected individuals are at risk for psychiatric disorders such as depression and PTSD [12-16]. In the South African context, PTSD is not an uncommon disorder in individuals with HIV/AIDS. In some cases, PTSD is secondary to the diagnosis of HIV/AIDS but in most cases it is seen after other traumas [15]. In addition, evidence suggests that major depressive disorder is more likely to be associated with PTSD in HIV infected individuals [15].
Prior studies have examined effects of resilience on adult psychopathology [20, 23] and depressive symptom severity [38] in individuals with childhood abuse and/or other trauma exposure. However, this is the first study, to our knowledge, to explore the relationship between resilience and depression in a cohort of HIV-infected women with childhood trauma and to find evidence of a mediating effect of posttraumatic symptoms on this

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relationship. In light of the study findings, it is important to screen not only for depression but also for comorbid posttraumatic stress symptoms in HIV-infected individuals and to develop interventions that enhance resilience among these individuals.

The results of the present study should be interpreted in light of the study limitations, including potential recall bias on the retrospective rating scales, the cross-sectional study design and the potential confounding effect of comorbid psychiatric disorders. In addition, no data on non-traumatic everyday stressful life events were captured.

Future studies with longitudinal assessment of this hypothesis are needed. Understanding how resilience can be enhanced is of great importance to not only promoting coping mechanisms but also alleviating maladaptive coping and stress responses in common mental illnesses such as depression and PTSD [26].

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Acknowledgements

We would like to acknowledge Professor Martin Kidd for providing statistical assistance.

Funding

This work is supported by the South African Research Chair in PTSD hosted by Stellenbosch University, funded by the DST and administered by NRF, the Claude Leon Foundation and the South African Medical Research Council.

Contributors

SS made substantial contributions to the conception and design, analysis of data, revising the manuscript and providing final approval of the version to be published. GS made a substantial contribution to conception and design, acquisition of data, analysis and interpretation of data, drafting and revising the article and providing final approval of the version to be published. All authors listed on the manuscript met all ICMJE criteria for authorship.

Funding

This work is supported by the South African Research Chair in PTSD hosted by Stellenbosch University, funded by the DST and administered by NRF, the Claude Leon Foundation and the South African Medical Research Council.

Competing interests

We declare we have no competing interests.

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Figure 1. Mediation model

Figure 2. PLS path analysis for all variables of interest.

REFERENCES

1 UNAIDS. Worlwide HIV & AIDS statistics. http://www.avert.org/worldstats.htm. Accessed September 09, 2013.

2 Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: relevance for HIV prevention in hyperendemic countries of southern Africa. *AIDS* 2008;**22**:73-86.

3 Jewkes R, Penn-Kekana L, Levin J, et al. Prevalence of emotional, physical and sexual abuse of women in three South African provinces. *S Afr Med J* 2001; **91**:421-428.

4 Kalichman SC, Simbayi LC. Sexual assault history and risks for sexually transmitted infections among women in an African township in Cape Town, South Africa. *AIDS Care* 2004;**16**:681-689.

5 Wilson HW, Widom CS. An examination of risky sexual behavior and HIV in victims of child abuse and neglect: a 30-year follow-up. *Health Psychol* 2008;**27**:149-158.

6 Crepaz N, Passin WF, Herbst JH, et al. Meta-analysis of cognitive-behavioral interventions on HIV-positive persons' mental health and immune functioning. *Health Psychol* 2008;**27**:4-14.

7 Bing EG, Burnam MA, Longshore D, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Arch Gen Psychiatry* 2001;**58**:721-728.

For peer review only

8 Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 2001;**158**:725-730.

9 Morrison MF, Petitto JM, Ten Have T, et al. Depressive and anxiety disorders in women with HIV infection. *Am J Psychiatry* 2002; **159**:789-796.

10 Rabkin JG, Johnson J, Lin SH, et al. Psychopathology in male and female HIV-positive and negative injecting drug users: longitudinal course over 3 years. *AIDS* 1997;**11**:507-515.

11 Cruess DG, Evans DL, Repetto MJ, et al. Prevalence, diagnosis, and pharmacological treatment of mood disorders in HIV disease. *Biol Psychiatry* 2003;**54**:307-316.

12 Myer L, Smit J, Roux LL, et al. Common Mental Disorders among HIV-Infected Individuals in South Africa: Prevalence, Predictors, and Validation of Brief Psychiatric Rating Scales. *AIDS Patient Care & STDs* 2008;**22**:147-158.

13 Olley BO, Gxamza F, Seedat S, et al. Psychopathology and coping in recently diagnosed HIV. *S Afr Med J* 2003;**93**:928-931.

14 Olley BO, Seedat S, Nei DG, et al. Predictors of Major Depression in Recently Diagnosed Patients with HIV/AIDS in South Africa. *AIDS Patient Care & STDs* 2004;**18**:481-487.

15 Olley BO, Zeier MD, Seedat S, et al. Post-traumatic stress disorder among recently diagnosed patients with HIV/AIDS in South Africa. *AIDS Care* 2005;**17**:550-557.

16 Olley BO, Seedat S, Stein DJ. Persistence of psychiatric disorders in a cohort of HIV/AIDS patients in South Africa: A 6-month follow-up study. *J Psychosom Res* 2006;**61**:479-484.

17 Spies G, Afifi TO, Archibald SL, et al. Mental health outcomes in HIV and childhood maltreatment: a systematic review. *Syst Rev* 2012;**1**:1-30.

For peer review only

18 Alim TN, Graves E, Mellman TA, et al. Trauma exposure, posttraumatic stress disorder and depression in an African-American primary care population. *J Natl Med Assoc* 2006;**98**:1630-1636.

19 Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. *Depress Anxiety* 1999;**9**:169-174.

20 Collishaw S, Pickles A, Messer J, et al. Resilience to adult psychopathology following childhood maltreatment: evidence from a community sample. *Child Abuse Negl* 2007;**31**:211-229.

21 Lizardi H, Klein DN, Ouimette PC, et al. Reports of the childhood home environment in early-onset dysthymia and episodic major depression. J *Abnorm Psychol* 1995;**104**:132-139.

22 Ritchie K, Jaussent I, Stewart R, et al. Association of adverse childhood environment and 5-HTTLPR Genotype with late-life depression. *J Clin Psychiatry* 2009;**70**:1281-1288.

23 Alim TN, Feder A, Graves REet al. Trauma, resilience, and recovery in a high-risk African-American population. *Am J Psychiatry* 2008;**165**:1566-1575.

24 Feder A, Nestler EJ, Charney DS. Psychobiology and molecular genetics of resilience. *Nat Rev Neurosci* 2009;**10**:446-457.

25 Southwick SM, Charney DS. The science of resilience: implications for the prevention and treatment of depression. *Science* 2012;**338**:79-82.

26 Wu G, Feder A, Cohen H, et al. Understanding resilience. *Front Behav Neurosci* 2013;**7**:10-25.

For peer review only

27 Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety* 2003;**18**:76-82.

28 Enns MW, Cox BJ. Psychosocial and clinical predictors of symptom persistence vs remission in major depressive disorder. *Can J Psychiatry* 2005;**50**:769-777.

29 Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *Am J Psychiatry* 2012; **169**:141-151.

30 Davidson JR, Payne VM, Connor KM, et al. Trauma, resilience and saliostasis: effects of treatment in post-traumatic stress disorder. *Int Clin Psychopharmacol* 2005;**20**:43-48.

31 Min JA, Lee NB, Lee CU, et al. Low trait anxiety, high resilience, and their interaction as possible predictors for treatment response in patients with depression. *J Affect Disord* 2012;**137**:61-69.

32 Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;**59**:22-33.

33 Radloff SF. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement* 1977;**1**:385-401.

34 Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric Properties of the Life Events Checklist. *Assessment* 2004;**11**:330-341.

35 Davidson JRT, Book SW, Colket JT, et al. Assessment of a new self-rating scale for post-traumatic stress disorder. *Psychol Med* 1997;**27**:153-160.

For peer review only

36 Bernstein DP, Stein JA, Newcomb MD, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl* 2003;**27**:169-190.

37 Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**:1173-1182.

38 Wingo AP, Wrenn G, Pelletier T, et al. Moderating effects of resilience on depression in individuals with a history of childhood abuse or trauma exposure. *J Affect Disord* 2010;**126**:411-414.

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DEPRESSION AND RESILIENCE IN HIV-INFECTED WOMEN WITH EARLY LIFE STRESS: DOES TRAUMA PLAY A MEDIATING ROLE? A CROSS-SECTIONAL STUDY.

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Keywords: HIV/AIDS, Depression, trauma, resilience, mediation

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ABSTRACT

Objectives: The present study sought to assess the relationship between depressive symptomatology and resilience among HIV-infected women and to investigate whether trauma exposure (childhood trauma, other discrete lifetime traumatic events) or the presence of posttraumatic stress symptomatology mediated this relationship.

Design: Cross-sectional study.

Setting: Western Cape, South Africa.

Participants: A convenience sample of 95 HIV-infected women in peri-urban communities in the Western Cape, South Africa. All the women had exposure to moderate to severe childhood trauma as determined by the Childhood Trauma Questionnaire.

Primary and secondary outcome measures: We examined the relationship between depressive symptomatology and resilience (the Connor-Davidson Resilience Scale) and investigated whether trauma exposure or the presence of posttraumatic stress symptomatology mediated this relationship through the Sobel test for mediation and PLS path analysis.

Results: There was a significant negative correlation between depressive symptomatology and resilience (p = < .01). PLS path analysis revealed a significant direct effect between depression and resilience. On the Sobel test for mediation, distal (childhood trauma) and proximal traumatic events did not significantly mediate this association (p = > .05). However, posttraumatic stress symptomatology significantly mediated the relationship between depression and resilience in trauma exposed women living with HIV.

Conclusions: In the present study, higher levels of resilience ~~resulted in~~were associated with lower levels of self-reported depression. Although causal inferences are not possible, this

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suggests that in this sample, resilience may act as protective factor against the development of clinical depression. The results also indicate that posttraumatic stress symptoms (PTSS), which are highly prevalent in HIV-infected and trauma exposed individuals and often comorbid with depression, may further explain and account for this relationship. Further investigation is required to determine if early identification and treatment of PTSS in this population may ameliorate the onset and persistence of major depression.

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ARTICLE SUMMARY

Strengths and limitations of this study

- This is the first study investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals and to find evidence of a mediating effect of posttraumatic symptoms on this relationship
- Potential recall bias on the retrospective rating scales may influence the findings.
- The cross-sectional study design precludes causal inferences and longitudinal assessment of this relationship is necessary.

BACKGROUND

In South Africa, an estimated 5.63 million individuals are infected with human immunodeficiency virus (HIV). Of these, 3.3 million are females [1]. High rates of intimate partner violence (IPV), rape, and childhood abuse have been reported [2-4]. Studies suggest high rates of childhood emotional (51.9%), physical (51.1%), and sexual (41.6%) abuse in HIV-positive individuals [5]. HIV has become a manageable chronic disease with the

increased use of highly active antiretroviral therapies (HAART). However, this chronicity is coupled with an increase in the number of lifetime emotional and physical challenges faced by infected individuals [6]. Common mental disorders such as depression and anxiety are highly prevalent and comorbid with HIV/AIDS. Compared to the general population and comparable HIV-negative individuals, evidence suggests that the prevalence of depression is two to four fold higher in HIV-infected individuals [7-10]. Prevalence rates of depression in HIV-positive individuals range from 5% to 20% across a majority of studies [11]. In South African studies, high rates of depression and posttraumatic stress disorder (PTSD) have been reported among HIV-infected individuals [12-16]. The most commonly reported psychiatric disorders among HIV-positive individuals with a history of childhood maltreatment include substance abuse, major depressive disorder, and posttraumatic stress disorder [17]. Research shows that childhood abuse and exposure to other traumas are among the risk factors for the development of adult psychopathology [18-22]. However, not every individual who experiences early life stress or other traumatic incidents will develop a psychiatric disorder, highlighting the importance of resilience [23, 24]. Human responses to stress and trauma differ widely. Some individuals develop psychiatric disorders, such as PTSD and depression; others develop psychological symptoms that resolve rapidly, while others report no symptoms in response to traumatic stress [25]. Numerous risk and protective factors, including developmental, cognitive, psychological (e.g. personality traits, coping style, social support) genetic, epigenetic and neurobiological (neurochemistry and neural circuitry) mechanisms, have been shown to play a role in how individuals respond to stress and trauma [25, 26]. Resilience is a multidimensional construct and is understood as an individual's ability to bounce back from hardship and trauma [25]. Resilience refers to a person's ability to adapt successfully to acute stress, trauma or more chronic forms of

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adversity [24]. Resilience represents the personal qualities that enable one to thrive in the face of adversity [27]. Resilience may be viewed as a measure of stress coping ability and, as such, could be an important target of treatment in anxiety, depression, and stress reactions [27]. However, there is relatively little awareness about resilience and its relationship to these disorders. In non-HIV samples, traumatic experiences such as childhood maltreatment and adult life stress, have been reported, among depressed patients, to influence treatment response [28, 29]. In patients with PTSD, high resilience has been associated with favourable treatment outcomes [30]. Recent data also indicates that in depressed patients resilience contributes to more favourable treatment outcomes with the effects of resilience even more definitive when combined with low trait anxiety [31].

To our knowledge, there are no studies investigating the relationship between depressive symptomatology and resilience in a sample of trauma exposed HIV-infected individuals. In light of this, the present study sought to examine this relationship in a sample of trauma exposed HIV-infected women.

METHODS

Participants

A total of 230 HIV-infected and uninfected women, with and without trauma exposure consented to participate and were enrolled into a larger prospective cognitive and imaging study. Of these, 95 HIV-positive women had exposure to childhood trauma as defined on the Childhood Trauma Questionnaire (CTQ) and were included in the present study. A score of 41 and higher on the CTQ was used as the cut-off for exposure to childhood trauma.

Eligibility criteria included: willingness and ability to provide written informed consent, ability to read and write in either English or Afrikaans at 5th grade level, aged between 18

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and 65 years, medically well enough to undergo neuropsychological testing and MRI scanning. Exclusions included: a current or past history of schizophrenia, bipolar disorder or other psychotic disorders, current substance or alcohol abuse or dependence, significant previous head injury, demonstrated frank dementia on the International HIV Dementia Scale, current seizure disorders of any cause, history of CNS infections of neoplasms, hepatitis B positive status, and current use or use within the last month of any psychotropic medication.

Procedure

The study was approved by the ethics committee of Stellenbosch University, South Africa. All participants were recruited by a researcher or with the help of doctors and adherence counselors from community health care facilities in and around the Cape Town area. All participants who consented were screened for eligibility and childhood trauma exposure either in person at their clinic or telephonically. Those who met initial screening criteria subsequently underwent behavioural, neuromedical, neurocognitive and neuroimaging assessments at Stellenbosch University. Participants were reimbursed for their travel costs to the University on two separate occasions.

Measures

Demographic and clinical characteristics

Age, gender, marital status, ethnicity, years of education and employment status were captured. A comprehensive history was obtained from, and a general physical examination conducted in, all patients. Virologic markers of disease progression (CD4 lymphocyte count and viral loads) were obtained from blood samples.

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Psychiatric morbidity

Current and lifetime psychiatric disorders were evaluated using the MINI- International Neuropsychiatric Interview- Plus (M.I.N.I.-Plus) [32].

Depression

Participants were assessed for depressive symptomatology using the Center for Epidemiologic Studies Depression Scale (CES-D) [33]. The CES-D is a 20-item widely used self-report instrument designed to measure depressive symptomatology. The scale was specifically designed to measure depressive symptomatology in the general population, unlike previous depression scales which have been predominantly used in clinical populations. The CES-D emphasises the affective component of depressive symptomatology, namely depressed mood. Each item comprises a likert scale ranging from 0 to 3. A total score for the 20 items is obtained, with the lowest possible score being 0 and the highest possible score being 60. Higher scores are indicative of more severe depression.

Traumatic life events

Exposure to traumatic life events were assessed for using the Life Events Checklist (LEC) [34]. The LEC is a widely used measure of exposure to potentially traumatic events. It was developed in order to facilitate the diagnosis of posttraumatic stress disorder (PTSD). One of the LEC's unique features is that it enquires about various types of exposure to each potentially traumatic event. Therefore, the LEC elicits whether the participant experienced, witnessed, or learned of the traumatic event, a feature that other traumatic event measures do not possess. Participants rate their experience of each traumatic event listed on a likert

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scale. A total score is derived from the sum of experiencing and/or witnessing the event. Higher scores are indicative of the experience of more traumatic life events.

Posttraumatic stress symptomatology

Posttraumatic stress symptomatology was assessed using the Davidson Trauma Scale (DTS) [35]. The DTS is a widely used 17-item self-report and measures symptoms of PTSD on frequency and severity scales. The items are categorised according to the criteria set out in the DSM-IV: criteria B (intrusive re-experiencing) criteria C (avoidance and numbness) and criteria D (hyperarousal). For each item, the participant rates the frequency and severity during the previous week on 5-point (0 to 4) scales, with the lowest possible score being 0 and the highest possible score being 136. Higher scores are indicative of more PTSD symptoms.

Childhood trauma

The Childhood Trauma Questionnaire Short Form (CTQ-SF) [36], a 28-item self-report inventory that provides valid screening for histories of abuse and neglect was administered. It assesses five types of maltreatment including, emotional, physical, and sexual abuse, and emotional and physical neglect. These five subscales each consist of 5 items with scores ranging from 5 to 25. The overall trauma score ranges from 25 to 125 with higher scores indicating higher levels of childhood trauma (score of 25-31 = no trauma, score of 41-51 = low to moderate, 56-68 = moderate to severe, and 73-125 = severe to extreme).

Resilience

Resilience was assessed using the Connor Davidson Resilience Scale (CD-RISC) [27, 35]. The CD-RISC is a self-report measure of resilience consisting of 25 items. The content of the scale

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reflects hardiness, control, commitment, personal or collective goals, change or stress viewed as a challenge/opportunity, strengthening effect of stress, past successes, recognition of limits to control, engaging the support of others, self-efficacy, optimism, action orientation, self-esteem/confidence, adaptability, tolerance of negative affect, problem solving skills, humour in the face of stress, patience, faith and secure bonds to others. Examples of items include: "I am able to adapt when changes occur", "I have at least one close and secure relationship which helps me when I am stressed", "when there are no clear solutions to my problems, sometimes fate or God can help", "under pressure I stay focused and think clearly", "I try to see the humorous side of things when I am faced with problems." The scale rates participants over the past month with a total score of the CD-RISC varying from 0-100. The items are scored on a 5 point likert scale, with higher scores reflecting higher resilience.

Data Analysis

Data were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 20.0 and Statistica, version 11.0.

Basic statistical analyses were conducted, which included descriptive statistics. Spearman correlation and multiple linear regression analyses were carried out to assess the relationship between the variables of interest.

According to Baron and Kenny (1986), a variable functions as a mediator when it meets the following conditions: (1) variations in the levels of the independent variable (IV) significantly account for variations in the mediator variable (MV) [figure 1, path *a*], (2) variations in the MV significantly account for variations in the dependent variable (DV) [figure 1, path *b*], and

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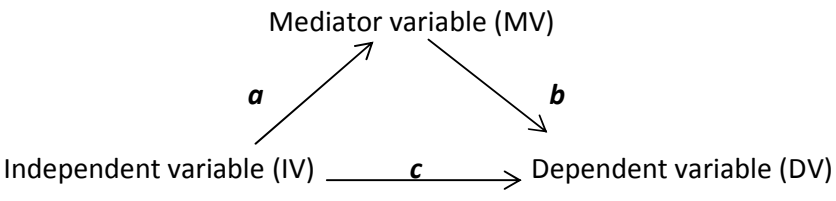
(3) when paths *a* and *b* are controlled for, a previous significant relation between the IV and DV is no longer significant, with the strongest demonstration of mediation occurring when path *c* (figure 1) is zero [37]. Rather than hypothesising a direct causal relationship between the IV and DV, a mediational model hypothesises that that IV influences the MV, which in turn influences the DV. In order to assess for a mediation effect, several steps were taken. Firstly, the Sobel test for mediation was conducted to assess whether childhood trauma, traumatic life events, or posttraumatic stress symptoms mediated the relationship between the dependent (depression) and independent variables (resilience). Secondly, to test for mediation, one should conduct three regression equations. Separate coefficients for each equation should be estimated and tested [37]. First, the MV should be regressed on the IV; second, the DV should be regressed on the IV; and third, the DV should be regressed on both the IV and the MV [37]. To establish mediation, the following conditions should be met: First, the IV must affect the MV in the first equation; second, the IV must be shown to affect the DV in the second equation; and third, the MV must affect the DV in the third equation. The effect of the IV on the DV should be less in the third equation than in the second. If the IV has no effect when the MV is controlled, then this is indicative of perfect mediation [37]. Lastly, a PLS path analysis was performed to confirm the results of the aforementioned analyses.

Figure 1. Mediation model



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RESULTS

Demographic characteristics of the sample

Participants were predominantly black (98.9%), Xhosa (African indigenous language) speaking (93.7%) women, with a mean age of 33.6 years (range 21-50). The mean highest level of education was 9.98 years, ranging from 5 to 14 years. The majority were single (73.7%), unemployed (70.5%), and reported a combined annual household income of less than $1,000 (10 000 ZAR) per year (87.4%).

Clinical characteristics of the sample

The mean CD4 lymphocyte count was 438.40 cells/mm^3 (range 25-1529 cells/mm^3). The mean HIV viral load was 106,157.05 copies/ml, ranging from below the detectable limit to 3,200,000 copies/ml. The lower limit for detection was 40 copies/ml. The predominant HIV clade was subtype C. Forty four (46%) of the women were on antiretroviral treatment (ARTs).

Depression, PTSD and resilience scores

The mean score on the CES-D was 17.7, with a minimum of 0 and a maximum of 60. The mean score on the DTS was 25.5, with a minimum of 0 and a maximum of 116. A total of 7 women (6.5%) met criteria for current MDD and 9 (8.4%) for recurrent MDD on the MINI-Plus. Two women (1.9%) met criteria for PTSD on the MINI-Plus. The mean score on the CD-RISC was 81.7 with a minimum of 24 and a maximum of 100, respectively.

Trauma exposure

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All women reported experiencing childhood trauma. The mean score on the CTQ was in the moderate to severe range (65.5), with a minimum of 41 and a maximum of 114. However, these women were also exposed to other discrete traumas regarded as index events for the development of PTSD. The commonest traumatic life events reported included: physical assault, transport accident, fire/explosion, life-threatening illness or injury and the sudden unexpected death of a loved one. Table 1 lists all the index traumas reported in this cohort of women.

Table 1. List of traumatic life events experienced (n = 95).

Index trauma (experienced or witnessed)	*Sum (n)*	*Percentage (%)*
Natural disaster	15	15.8
Fire/explosion	50	52.7
Transport accident	59	62.1
Serious accident at work, home or while doing sports	23	24.2
Physical assault	69	72.6
Assaulted with a weapon	52	54.7
Sexual assault	35	36.8
Other unwanted/uncomfortable sexual experience	17	17.9
Exposure in a war zone	8	8.5
Captivity (kidnapped, abducted, held hostage)	9	9.5
A life-threatening illness or injury	47	49.5
Exposure to sudden/violent death (murder, suicide)	24	25.3
Sudden or unexpected death of someone close	43	45.2
Serious injury, harm or death you caused to someone else	12	12.7
Badly beaten by parents or guardian as a child	23	24.2
Badly beaten by a spouse or partner	34	35.8
Other life-threatening experience not listed	8	8.5

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~~Reliability analysis~~Internal consistency

Cronbach alpha coefficients for all measures ranged from good to excellent: CTQ (α = .73), LEC (α = .78), DTS (α = .89), CD-RISC (α = .94), CES-D (α = .96).

Correlation between variable of interest

Pearson's correlation coefficients were calculated to assess the relationship between all the variables of interest. There was a significant negative correlation between depression (CES-D) and resilience (CD-RISC) scores, r = -0.28, p = < 0.01. In addition, there was a significant negative correlation between posttraumatic stress symptoms (DTS) and resilience (CD-RISC), r = -0.23, p = < 0.05. These correlations suggest that higher levels of resilience resulted in lower levels of self-reported depression and posttraumatic stress symptoms. Moreover, Pearson's correlation coefficients were calculated to assess the relationship between the IV and MV, and the MV and DV. The IV and DV were significantly correlated with two of the presumed MVs, namely childhood trauma (CTQ) and posttraumatic stress symptoms (DTS). However, traumatic life events (LEC) were not significantly correlated with either the IV or DV, suggesting that this variable is not a mediator (Table 2).

Table 2. Pearson's correlation coefficients for all variables of interest (n = 95).

Variable 1	Variable 2	Pearson r	p value
CTQ	CESD	0.23	0.02
CTQ	LEC	0.12	0.27
CTQ	DTS	-0.01	0.94
CTQ	CDRS	0.22	0.04
CESD	LEC	0.15	0.15

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CESD	DTS	0.48	<0.01
CESD	CDRS	-0.28	<0.01
LEC	DTS	0.18	0.08
LEC	CDRS	-0.02	0.84
DTS	CDRS	-0.23	0.03

CDRS = Connor Davidson Resilience Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DTS = Davidson Trauma Scale; CTQ = Childhood Trauma Scale; LE = Life Events Checklist.

Multiple linear regression

Multiple linear regression with depression (CES-D score) as the outcome variable revealed a significant model of 4 factors: childhood trauma (β =.330, p = .002), other trauma exposure (β = .181, p = .718), posttraumatic stress symptomatology (β =.216, p = .000), and resilience (β = -.236, p = .007), of which 3 of the 4 variables were significantly associated with depression (Table 3). This model explains 35% of the variance of depressive symptomatology (R^2= 0.35). As expected, childhood trauma and posttraumatic stress symptoms contributed to depression severity while resilience appeared to reduce it.

Table 3. Regression model for depressive symptomatology (CES-D score) (n = 95).

Variable	*df*	β	SE of β	*p*	R^2	Adjusted R^2
Model	4	-	-	.000	.347	.318
Childhood trauma (CTQ)	1	.330	.101	.002		
Other trauma (LEC)	1	.181	.499	.718		
Trauma symptoms (DTS)	1	.216	.045	.000		
Resilience (CD-RISC)	1	-.236	.085	.007		

Sobel test for mediation

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To assess for mediation, the Sobel test for mediation was performed. The results showed that neither childhood trauma [CTQ] (z = 1.77, p = 0.08) nor stressful life events [LEC] (z = -0.19, p = 0.84) significantly mediated the relationship between depression and resilience in this sample ~~(p > 0.05)~~. However, the results demonstrated that posttraumatic stress symptomatology (DTS) was a significant mediator (z = -2.03, p = 0.04~~p <0.05~~).

Regression analysis

To confirm whether posttraumatic stress symptomatology (MV) in fact mediated the relationship between depression (DV) and resilience (IV), three separate regression equations were conducted following the guidelines described in the data analysis section. The first regression equation showed that the IV significantly influenced the MV, (β = -.226, p = .027). The second regression equation showed that the IV significantly influenced the DV, (β = -.283, p = .005). The third regression equation showed that the MV significantly influenced the DV, (β = .442, p = .000). The effect of the IV on the DV was less in the third equation than in the second equation, β = -.183 (p = .049) vs. β = -.283 (p = .005). This is indicative of partial mediation. Posttraumatic stress symptoms accounts for some, but not all, of the relationship between depression and resilience. Partial mediation implies that there is not only a significant relationship between the mediator and the dependent variable, but also some direct relationship between the independent and dependent variable.

PLS path analysis

The PLS path analysis revealed a significant direct effect between depression and resilience ($p < .05$). The PLS path analysis also revealed that the effects via DTS (posttraumatic stress

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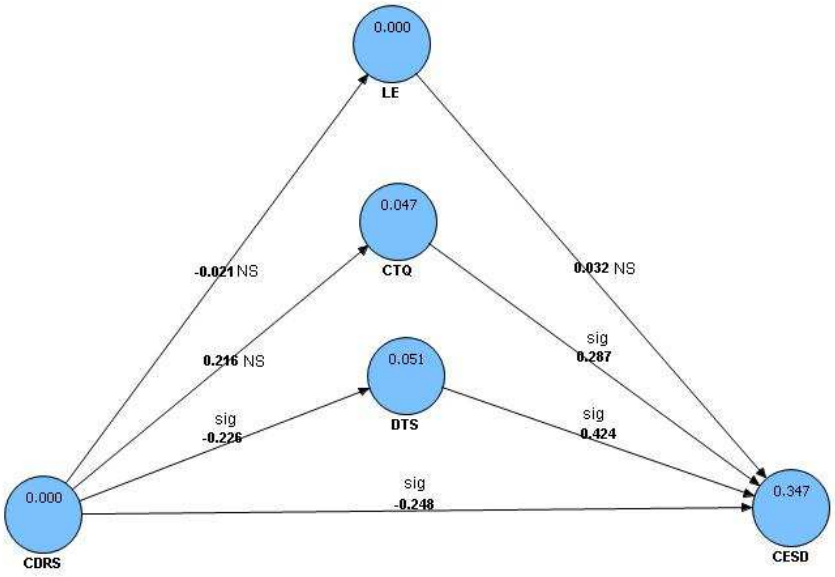
symptoms) were also significant ($p < .05$). This implies that although there is a mediating effect, there is also evidence of a direct effect. The other presumed mediators (CTQ and LEC) were not significant ($p > .05$). See figure 2.

Figure 2. PLS path analysis for all variables of interest.



CDRS = Connor Davidson Resilience Scale; CES-D = Center for Epidemiologic Studies Depression Scale; DTS = Davidson Trauma Scale; CTQ = Childhood Trauma Scale; LE = Life Events Checklist.

DISCUSSION

In this cross-sectional study of 95 HIV-infected women, we found that childhood trauma, posttraumatic stress symptoms and resilience independently predicted depressive symptoms. Childhood trauma and posttraumatic stress symptomatology contributed to depression, while resilience appeared to mitigate it. The results demonstrated a significant association between depression and resilience in this cohort, with resilience acting as a protective buffer. Posttraumatic stress symptoms were found to mediate this relationship and accounted for some, but not all, of the relationship between depression and resilience.

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A cut-off score of 16 or greater on the CES-D has been used to identify individuals at risk for clinical depression. Although, the mean score on the CES-D for this cohort was 17.7, this score is still relatively low. Results revealed a significant negative association between depression and resilience in this cohort of women, suggesting that resilience may be acting as a protective buffer against the development of clinically significant depression. The mean score on the CD-RISC was 81.7, suggesting high levels of resilience.

Childhood trauma and posttraumatic stress symptoms independently predicted depressive symptoms but other traumatic life events did not. Mediation analyses demonstrated that childhood trauma did not mediate the relationship between depression and resilience but posttraumatic stress symptoms did. This suggests that it is not the experience of trauma itself that contributes to depression per se, but the psychological manifestation thereof, in this case posttraumatic stress symptoms. A score of 40 and greater has been used to identify individuals with clinically significant PTSD. The mean score on the DTS in this cohort was substantially lower (25.5), once again highlighting the possible role of resilience in this cohort of women. This mediational model suggests that in this cohort, resilience influences (reduces) posttraumatic stress symptoms, which in turn influences (reduces) depressive symptoms. However, this is a partial mediation, suggesting that there is also evidence of a direct link between depression and resilience. Resilience appears to act as a protective buffer against depression, irrespective of the mediating role of posttraumatic stress symptoms.

The finding that childhood trauma and posttraumatic stress symptoms were each associated with depression is in keeping with other studies. Given that these women all reported early life stress and a number of other traumatic life events, this finding was expected. HIV-

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infected individuals are at risk for psychiatric disorders such as depression and PTSD [12-16]. In the South African context, PTSD is not an uncommon disorder in individuals with HIV/AIDS. In some cases, PTSD is secondary to the diagnosis of HIV/AIDS but in most cases it is seen after other traumas [15]. In addition, evidence suggests that major depressive disorder is more likely to be associated with PTSD in HIV infected individuals [15].

Prior studies have examined effects of resilience on adult psychopathology [20, 23] and depressive symptom severity [38] in individuals with childhood abuse and/or other trauma exposure. However, this is the first study, to our knowledge, to explore the relationship between resilience and depression in a cohort of HIV-infected women with childhood trauma and to find evidence of a mediating effect of posttraumatic symptoms on this relationship. In light of the study findings, it is important to screen not only for depression but also for comorbid posttraumatic stress symptoms in HIV-infected individuals and to develop interventions that enhance resilience among these individuals.

The results of the present study should be interpreted in light of the study limitations, including potential recall bias on the retrospective rating scales, the cross-sectional study design and the potential confounding effect of comorbid psychiatric disorders. In addition, no data on non-traumatic everyday stressful life events were captured.

Future studies with longitudinal assessment of this hypothesis are needed. Understanding how resilience can be enhanced is of great importance to not only promoting coping mechanisms but also alleviating maladaptive coping and stress responses in common mental illnesses such as depression and PTSD [26].

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Acknowledgements

We would like to acknowledge Professor Martin Kidd for providing statistical assistance.

Contributors

SS made substantial contributions to the conception and design, analysis of data, revising the manuscript and providing final approval of the version to be published. GS made a substantial contribution to conception and design, acquisition of data, analysis and interpretation of data, drafting and revising the article and providing final approval of the version to be published. All authors listed on the manuscript met all ICMJE criteria for authorship.

Funding

This work is supported by the South African Research Chair in PTSD hosted by Stellenbosch University, funded by the DST and administered by NRF, the Claude Leon Foundation and the South African Medical Research Council.

Competing interests

We declare we have no competing interests.

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REFERENCES

1 UNAIDS. Worlwide HIV & AIDS statistics. http://www.avert.org/worldstats.htm. Accessed September 09, 2013.

2 Andersson N, Cockcroft A, Shea B. Gender-based violence and HIV: relevance for HIV prevention in hyperendemic countries of southern Africa. *AIDS* 2008;**22**:73-86.

3 Jewkes R, Penn-Kekana L, Levin J, Ratsaka M, Schrieber M. Prevalence of emotional, physical and sexual abuse of women in three South African provinces. *S Afr Med J* 2001; **91**:421-428.

4 Kalichman SC, Simbayi LC. Sexual assault history and risks for sexually transmitted infections among women in an African township in Cape Town, South Africa. *AIDS Care* 2004;**16**:681-689.

5 Wilson HW, Widom CS. An examination of risky sexual behavior and HIV in victims of child abuse and neglect: a 30-year follow-up. *Health Psychol* 2008;**27**:149-158.

6 Crepaz N, Passin WF, Herbst JH, Rama SM, Malow RM, Purcell DW, et al. Meta-analysis of cognitive-behavioral interventions on HIV-positive persons' mental health and immune functioning. *Health Psychol* 2008;**27**:4-14.

7 Bing EG, Burnam MA, Longshore D, Fleishman JA, Sherbourne CD, London AS, et al. Psychiatric disorders and drug use among human immunodeficiency virus-infected adults in the United States. *Arch Gen Psychiatry* 2001;**58**:721-728.

8 Ciesla JA, Roberts JE. Meta-analysis of the relationship between HIV infection and risk for depressive disorders. *Am J Psychiatry* 2001;**158**:725-730.

For peer review only

9 Morrison MF, Petitto JM, Ten Have T, Gettes DR, Chiappini MS, Weber AL, et al. Depressive and anxiety disorders in women with HIV infection. *Am J Psychiatry* 2002; **159**:789-796.

10 Rabkin JG, Johnson J, Lin SH, Lipsitz JD, Remien RH, Williams JB, et al. Psychopathology in male and female HIV-positive and negative injecting drug users: longitudinal course over 3 years. *AIDS* 1997;**11**:507-515.

11 Cruess DG, Evans DL, Repetto MJ, Gettes D, Douglas SD, Petitto JM. Prevalence, diagnosis, and pharmacological treatment of mood disorders in HIV disease. *Biol Psychiatry* 2003;**54**:307-316.

12 Myer L, Smit J, Roux LL, Parker S, Stein DJ, Seedat S. Common Mental Disorders among HIV-Infected Individuals in South Africa: Prevalence, Predictors, and Validation of Brief Psychiatric Rating Scales. *AIDS Patient Care & STDs* 2008;**22**:147-158.

13 Olley BO, Gxamza F, Seedat S, Theron H, Taljaard J, Reid E, et al. Psychopathology and coping in recently diagnosed HIV. *S Afr Med J* 2003;**93**:928-931.

14 Olley BO, Seedat S, Nei DG, Stein DJ. Predictors of Major Depression in Recently Diagnosed Patients with HIV/AIDS in South Africa. *AIDS Patient Care & STDs* 2004;**18**:481-487.

15 Olley BO, Zeier MD, Seedat S, Stein DJ. Post-traumatic stress disorder among recently diagnosed patients with HIV/AIDS in South Africa. *AIDS Care* 2005;**17**:550-557.

16 Olley BO, Seedat S, Stein DJ. Persistence of psychiatric disorders in a cohort of HIV/AIDS patients in South Africa: A 6-month follow-up study. *J Psychosom Res* 2006;**61**:479-484.

For peer review only

17 Spies G, Afifi TO, Archibald SL, Fennema-Notestine C, Sareen J, Seedat S. Mental health outcomes in HIV and childhood maltreatment: a systematic review. *Syst Rev* 2012;**1**:1-30.

18 Alim TN, Graves E, Mellman TA, Aigbogun N, Gray E, Lawson W, et al. Trauma exposure, posttraumatic stress disorder and depression in an African-American primary care population. *J Natl Med Assoc* 2006;**98**:1630-1636.

19 Bernet CZ, Stein MB. Relationship of childhood maltreatment to the onset and course of major depression in adulthood. *Depress Anxiety* 1999;**9**:169-174.

20 Collishaw S, Pickles A, Messer J, Rutter M, Shearer C, Maughan B. Resilience to adult psychopathology following childhood maltreatment: evidence from a community sample. *Child Abuse Negl* 2007;**31**:211-229.

21 Lizardi H, Klein DN, Ouimette PC, Riso LP, Anderson RL, Donaldson SK. Reports of the childhood home environment in early-onset dysthymia and episodic major depression. J *Abnorm Psychol* 1995;**104**:132-139.

22 Ritchie K, Jaussent I, Stewart R, Dupuy AM, Courtet P, Ancelin ML, et al. Association of adverse childhood environment and 5-HTTLPR Genotype with late-life depression. *J Clin Psychiatry* 2009;**70**:1281-1288.

23 Alim TN, Feder A, Graves RE, Wang Y, Weaver J, Westphal M, et al. Trauma, resilience, and recovery in a high-risk African-American population. *Am J Psychiatry* 2008;**165**:1566-1575.

24 Feder A, Nestler EJ, Charney DS. Psychobiology and molecular genetics of resilience. *Nat Rev Neurosci* 2009;**10**:446-457.

For peer review only

25 Southwick SM, Charney DS. The science of resilience: implications for the prevention and treatment of depression. *Science* 2012;**338**:79-82.

26 Wu G, Feder A, Cohen H, Kim JJ, Calderon S, Charney DS, et al. Understanding resilience. *Front Behav Neurosci* 2013;**7**:10-25.

27 Connor KM, Davidson JR. Development of a new resilience scale: the Connor-Davidson Resilience Scale (CD-RISC). *Depress Anxiety* 2003;**18**:76-82.

28 Enns MW, Cox BJ. Psychosocial and clinical predictors of symptom persistence vs remission in major depressive disorder. *Can J Psychiatry* 2005;**50**:769-777.

29 Nanni V, Uher R, Danese A. Childhood maltreatment predicts unfavorable course of illness and treatment outcome in depression: a meta-analysis. *Am J Psychiatry* 2012; **169**:141-151.

30 Davidson JR, Payne VM, Connor KM, Foa EB, Rothbaum BO, Hertzberg MA, et al. Trauma, resilience and saliostasis: effects of treatment in post-traumatic stress disorder. *Int Clin Psychopharmacol* 2005;**20**:43-48.

31 Min JA, Lee NB, Lee CU, Lee C, Chae JH. Low trait anxiety, high resilience, and their interaction as possible predictors for treatment response in patients with depression. *J Affect Disord* 2012;**137**:61-69.

32 Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry* 1998;**59**:22-33.

For peer review only

33 Radloff SF. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. *Applied Psychological Measurement* 1977;**1**:385-401.

34 Gray MJ, Litz BT, Hsu JL, Lombardo TW. Psychometric Properties of the Life Events Checklist. *Assessment* 2004;**11**:330-341.

35 Davidson JRT, Book SW, Colket JT, Tupler LA, Roth S, David D, et al. Assessment of a new self-rating scale for post-traumatic stress disorder. *Psychol Med* 1997;**27**:153-160.

36 Bernstein DP, Stein JA, Newcomb MD, Walker E, Pogge D, Ahluvalia T, et al. Development and validation of a brief screening version of the Childhood Trauma Questionnaire. *Child Abuse Negl* 2003;**27**:169-190.

37 Baron RM, Kenny DA. The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986;**51**:1173-1182.

38 Wingo AP, Wrenn G, Pelletier T, Gutman AR, Bradley B, Ressler KJ. Moderating effects of resilience on depression in individuals with a history of childhood abuse or trauma exposure. *J Affect Disord* 2010;**126**:411-414.

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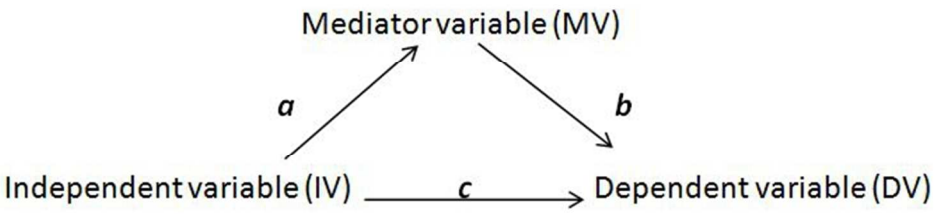
Figure 1. Mediation model



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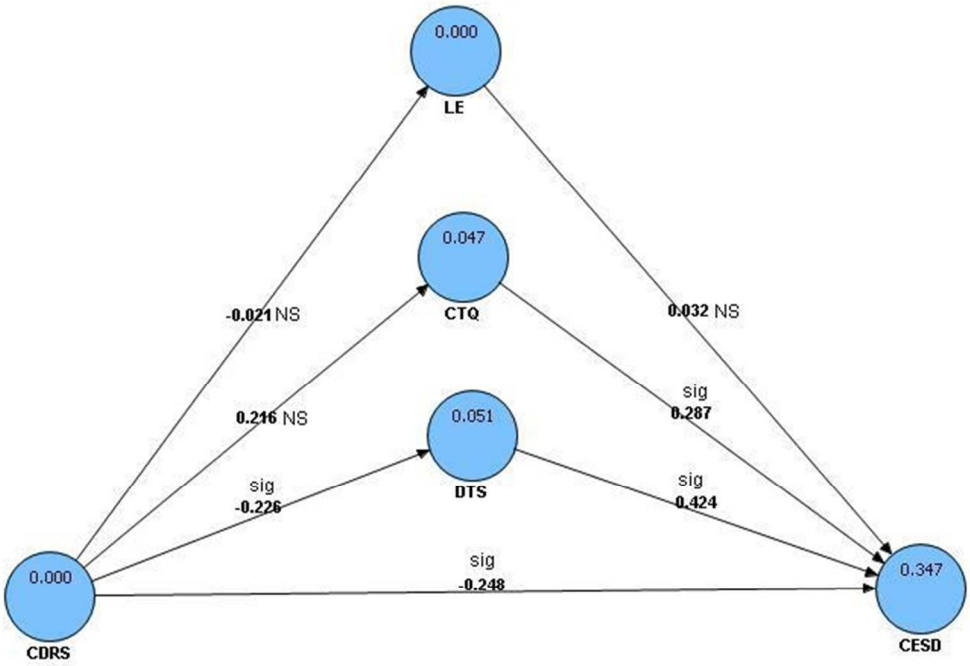

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