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Pain in Clients Attending a South African Voluntary Counseling and Testing Center Was Frequent and Extensive But Did Not Depend on HIV Status

Antonia L. Wadley, PhD,[a] Erica Lazarus, MB BCh,[b] Glenda E. Gray, MB BCh,[b,c] Duncan Mitchell, PhD,[a] and Peter R. Kamerman, PhD[a,d]

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Background: The frequency of pain is reported to be high in people living with HIV, but valid comparisons between people living with HIV and HIV-negative cohorts are rare. We investigated whether HIV infection influenced frequency and characteristics of pain in adults undergoing voluntary testing for HIV.

Setting: Participants were recruited from an HIV voluntary counseling and testing center at the Chris Hani Baragwanath Academic Hospital, Soweto, South Africa.

Methods: Pain was assessed using the Wisconsin Brief Pain Questionnaire. Depressive and anxiety symptomatology was determined using the Hopkins Symptom checklist-25. We then stratified by HIV status.

Results: Data from 535 black South Africans were analyzed: HIV-infected n = 70, HIV-uninfected n = 465. Overall, frequency of any current pain was high with 59% [95% confidence interval (CI): 55 to 63, n: 316/535] of participants reporting pain, with no difference related to HIV status: HIV-infected 50% (95% CI: 37 to 61, n: 35/70), HIV-uninfected 60% (95% CI: 56 to 65, n: 281/465). Pain intensity and number of pain sites were similar between the groups as were symptoms of anxiety and depression: mean Hopkins Symptom Checklist-25 1.72 (95% CI: 1.57 to 1.87) HIV-infected participants and 1.68 (95% CI: 1.63 to 1.73) HIV-uninfected participants. Univariate analysis showed female sex and greater depressive and anxiety symptomatology associated with pain. In a multivariable modeling, only depressive and anxiety symptomatology was retained in the model.

Conclusion: The high frequency of pain found in both HIV-infected and HIV-uninfected individuals presenting at a voluntary counseling and testing center was more likely to be associated with depression and anxiety, than with the presence or absence of HIV.

Key Words: HIV, pain, depression, anxiety

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INTRODUCTION

The reported prevalence of pain in cohorts of ambulatory people living with HIV (PLWH) ranges from 54% to 81% compared with the general population prevalence of around 35%.[1–5] Possible reasons for the increased prevalence of pain in PLWH are that, in addition to pains that affect the general population, for example, lower back pain and arthritic pain, PLWH have the additional burden of pain directly related to the infection itself, secondary infective and non-infective diseases, increased proinflammatory cytokines, and iatrogenic causes.[6–8] Although pain severity in PLWH seems to be worse in those with late-stage HIV/AIDS,[9,10] data supporting an association between pain and immunological suppression or viral load are equivocal.[5,8,11,12] Thus, treating HIV is not necessarily sufficient to treat the additional burden of pain.

Demographic factors such as female sex-at-birth and lower levels of education, and psychosocial factors such as depression, substance use, trauma, and lower levels of social support (for review see Refs. 5 and 13) that are associated with pain in the general population are also associated with pain in PLWH. However, there is little information comparing PLWH with HIV-uninfected people in similar sociocultural and economic conditions, to establish the degree to which physiological, demographic, and sociocultural factors contribute to the high pain prevalence in PLWH. One reason for the paucity of information is the difficulty of constructing a control group matching PLWH not just physiologically, socially, and demographically, but also psychologically, given the inevitable psychological burden of confirmed HIV infection.

We undertook a prospective cross-sectional study to determine the effect of HIV status on frequency and burden of

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pain in adults in Soweto, South Africa. As other studies have shown a greater frequency of pain in cohorts with HIV compared with general populations,[1–3,5] our primary hypothesis was that HIV infection would be associated with greater frequency of pain. Also, because PLWH reported greater pain intensity than people in the general population[1,9,14] and experimental evidence suggests that HIV may sensitize individuals to pain,[11] we formulated a secondary hypothesis that HIV infection would increase the overall burden of pain, as assessed by pain intensity, location, and number of pain sites. We also analyzed social and demographic factors that might influence the frequency of pain. By assessing pain in clients attending a voluntary counseling and testing (VCT) center before they knew their HIV status, we hoped to match the psychological state of the control group to that of PLWH.

METHODS

Setting

Between 19 August 2013 and 20 May 2015, a convenience sample of adult participants of African ancestry was recruited from a HIV VCT center at the Perinatal HIV Research Unit in Soweto, South Africa. Soweto is located in Gauteng province where HIV infection prevalence at the time was 12.8%.[15]

Participants

Clients who were attending the center for routine HIV testing were eligible if they were 18 years or older, unaware of their current HIV status, and able to provide informed consent.

The study was approved by the Human Ethics Research Committee (Medical), University of the Witwatersrand, South Africa (clearance number: M130542). All participants provided written informed consent before undergoing any procedures. Participants were compensated in the form of ZAR 20 in "air-time" credit for their mobile phones.

Measures

After providing consent, and before undergoing counseling and HIV testing, participants were interviewed to assess their pain. Trained interviewers used standardized questionnaires originally developed in English and subsequently translated and validated for use in isiZulu and Setswana.[16,17] The consenting process and the interview took place in a private examination room at the testing center. To account for variations in participants' ability to self-complete questionnaires, the interviewer asked all the participants questions verbally and recorded the participants' answers on printed forms.

Sociodemographic Data

The following variables were elicited in the interview: self-declared binary sex (male or female), age (years), education (formal schooling: yes or no, and if "yes," highest school grade and postschool qualification achieved), employment status (full-time employment, part-time employment/piece work, unemployed), and receipt of government social grants in lieu of employment income (old-age pension and disability grant). The outcome of each participant's HIV antibody tests, and, if they tested positive, CD4 T-cell count, was obtained later from their medical records, with the permission of the participants.

Pain, Depression, and Anxiety Assessment

We characterized pain using the Wisconsin Brief Pain Questionnaire.[16,18] This scale has been validated and has been well used in South African second-language English speakers.[9,14,16,17] The questionnaire assessed the presence and characteristics of pain including distribution and intensity of pain. For the primary outcome—frequency of pain—we identified the participants as having pain, or not, according to how they responded to 2 questions: (1) Have you had pain in the last month? (2) rate your pain at its worst in the past week (assessed on an 11-point numerical pain rating scale anchored at 0 = no pain and 10 = pain as bad as you can imagine). We classified participants as having pain if they answered "yes" to the first question and they rated their worst pain in the past week as being greater than zero. For pain-site distribution, we substituted a tick-box list of body parts potentially affected by pain for the body chart cartoon on the original questionnaire, and we asked participants to identify which affected site was the source of their worst pain.

We assessed depression and anxiety using the Hopkins Symptom Checklist (HSCL)-25, which is a checklist of 15 depression-related and 10 anxiety-related symptoms, with the presence and severity of each symptom in the past week being rated on a 4-point rating scale anchored at 1 = not at all and 4 = extremely distressed/bothered.[17,19,20] This scale has been previously used and validated in South Africa.[17,21] Depression and anxiety symptoms were analyzed separately and in a combined global score. Scoring involves taking the average score across the items being assessed, so scores range between 1 and 4, with 4 being "extremely distressed/bothered."

HIV Testing

HIV testing was performed according to the South African National Department of Health guidelines.[22] Presence or absence of HIV infection was diagnosed by 2 point-of-care rapid antibody screening tests using different test kits. If the results of the rapid tests were discordant, a confirmatory laboratory enzyme-linked immunosorbent assay was performed.

Data Analysis

All analyses were performed using R v3.6.0.[23]To calculate the sample size required to ensure 80% power to detect a difference in the frequency of pain between HIV-infected and HIV-uninfected people, we used a two-sided significance level of 95% with at most a 1:2 recruitment ratio of HIV-infected to HIV-uninfected individuals, based on an estimated 34% prevalence of pain in the HIV-uninfected group[3,24] and an estimated 56% prevalence of pain in the HIV-infected group.[9] These parameters yielded a minimum

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sample size of 63 HIV-infected individuals and 126 HIV-uninfected individuals.

All data are reported as mean, median, or percentage with a 95% confidence interval (CI). Differences between the HIV-infected and HIV-uninfected groups for frequency of pain, sociodemographic characteristics (eg, age, schooling, and employment), and pain characteristics (eg, pain intensity and number of pain sites) were assessed using 95% CIs of the difference in mean/percentage. These intervals were interpreted based on whether they included 0, the distance of the lower or upper limit from 0 (when the interval excluded 0), and the width of the interval. All CIs were bootstrap intervals calculated from 999 resamples using the percentile method.

We examined univariate risk factors for having pain using logistic regression with pain/no pain as the dependent variable. Multivariable logistic regression modeling, with pain/no pain as the dependent variable, was undertaken using backward variable elimination with Akaike's information criterion as a stopping rule. Stability of the model was assessed by performing the backward elimination procedure on 100 bootstrapped resamples.

Full analysis scripts can be accessed at https://github.com/kamermanpr/HIV-pain-VCT.git.

RESULTS

Informed consent was completed by 540 individuals. HIV test result data were missing for 5 participants, and thus, 535 were included in the final analysis: HIV-infected n = 70, HIV-uninfected n = 465; recruitment ratio: ~1:7.6. We achieved the required minimum number of HIV-infected participants and well exceeded the required number of HIV-uninfected participants.

Descriptive Data

Descriptive demographic and pain data for the whole cohort and stratified by HIV status are shown in Table 1 (also see Supplements 1 and 2, Supplemental Digital Content, http://links.lww.com/QAI/B407, http://links.lww.com/QAI/B407, respectively). On average, the HIV-infected group was slightly older than the HIV-uninfected group, and had lower levels of education, whereas very few participants in either group had fewer than 7 years of schooling. There were no differences in pain characteristics between the groups, but the pain burden was high. On average, participants had more than one pain site, with the head being the worst-affected site. The frequency of pharmacological management was >45% in both groups, and opioid use was rare. Nevertheless, there was a marginally greater use of weak opioids in the HIV-uninfected group compared with the infected group. Self-admitted use of alcohol or marijuana for pain relief was low in both groups.

Primary Outcome

The frequency of pain in the full cohort was 59% (n: 316/535; 95% CI: 55 to 63). The frequencies were 50% (n: 35/70; 95% CI: 37 to 61) for HIV-infected and 60% (n: 281/465; 95% CI: 56 to 65) for HIV-uninfected (Fig. 1, and see Supplement 3, Supplemental Digital Content, http://links.lww.com/QAI/B407). The CI for the difference in the frequency of pain between the 2 groups was 10% (95% CI: −2.0 to 24). The 95% CI included zero, indicating that the difference in point estimates of the frequency of pain in the 2 groups was not statistically significant.

As an exploratory analysis, we also examined whether the frequency of moderate-to-severe pain (pain rating >3 on the numerical pain rating scale)[25,26] differed between the HIV-infected and uninfected groups. There was no difference. The frequency of moderate-to-severe pain was 47% (n: 33/70; 95% CI: 34 to 59) for HIV-infected and 54% (n: 250/465; 95% CI: 49 to 59) for HIV-uninfected (see Supplement 3, Supplemental Digital Content, http://links.lww.com/QAI/B407). The CI for the difference in the frequency of moderate-to-severe pain between the 2 groups was 7% (95% CI: −6 to 20).

Risk Factors for Having Pain

Table 2 (also see Supplements 4 and 5, Supplemental Digital Content, http://links.lww.com/QAI/B407, http://links.lww.com/QAI/B407, respectively) shows the results of logistic regression models for individual predictors for having pain. Based on high levels of correlation between scores for the 2 dimensions of depression and anxiety, we only report the global score (see Supplement 1, Supplemental Digital Content, http://links.lww.com/QAI/B407). Of the factors that we investigated, only the total score for the HSCL-25 and being female were significantly associated with having pain. As the HSCL-25 score increased, and hence the severity of anxiety and depression symptomatology increased, likelihood of having pain increased. Similarly, female participants were more likely to have pain than were their male counterparts.

We included all 6 variables (HIV status, age, sex, education level, employment status, and HSCL-25 score) in a multivariable logistic regression with backward variable elimination. Table 3 (see Supplement 5, Supplemental Digital Content, http://links.lww.com/QAI/B407) reports the outcomes of the final model that we generated and has HSCL-25 total score as the only factor retained in the model. In the stability analysis, all 100 bootstrapped resamples retained HSCL-25 total score in the model, with other variables also retained depending on the particular sample (see Supplement 5, Supplemental Digital Content, http://links.lww.com/QAI/B407).

DISCUSSION

The main novelty of our study was that we assessed our hypotheses regarding the effect of HIV infection on the frequency, characteristics, and risk factors of pain in a cohort of people whose self-report of pain was not influenced by a previous knowledge of their HIV status. Because participants did not know their HIV status at the time of testing, psychosocial consequences of day-to-day living with HIV, such as dealing with the diagnosis, HIV-related health worries, or enacted or anticipated HIV stigma[27] could not have influenced the development of pain. In addition, since

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TABLE 1. Characteristics of the Cohort

Variable	Point Estimate (95% CI)*			
	Whole Cohort, n = 535	HIV-Infected, n = 70	HIV-Uninfected, n = 465	Difference in Mean/Frequency HIV+ minus HIV−
Demographic information:				
Age (yr, mean)†	34.3 (33.4 to 35.3)	36.8 (34.5 to 39.2)	33.9 (32.9 to 35.0)	2.8 (0.4 to 5.5)‡
CD4 T-cell count (cells/μL, median)†	—	436 (306 to 573)	—	—
Global Hopkins Symptom Checklist-25 (mean)†	1.68 (1.64 to 1.73)	1.72 (1.57 to 1.87)	1.68 (1.63 to 1.73)	0.04 (−0.12 to 0.22)
Female, %†	55 (51 to 59)	64 (52 to 75)	53 (49 to 85)	10 (−2 to 22)
Years of schooling, %†				
0–7	5 (3 to 6)	14 (6 to 23)	4 (2 to 5)	11 (3 to 20)‡
8–12	61 (58 to 66)	64 (53 to 74)	61 (57 to 66)	3 (−10 to 15)
>12	34 (30 to 38)	22 (11 to 31)	35 (31 to 40)	−14 (−25 to −4)‡
Employment, %†§				
Unemployed	51 (47 to 55)	57 (46 to 69)	50 (45 to 54)	7 (−5 to 20)
Employed	45 (41 to 50)	39 (27 to 50)	47 (42 to 51)	−8 (−20 to 4)
Pension/disability grant	4 (2 to 5)	4 (0 to 10)	3 (2 to 5)	1 (−4 to 7)
Estimated alcohol consumption (units/month)	3.5 (3.5 to 3.5)	3.5 (0.8 to 6.0)	3.5 (2.5 to 3.5)	0 (−3.5 to 2.5)
Pain information (only those with pain): $n_{(\text{whole cohort/HIV+/HIV}-)}$ = 316/35/281				
Pain the reason for being tested, %†	10 (6 to 13)	17 (6 to 29)	9 (5 to 12)	9 (−3 to 21)
Intensity of worst pain in the past week (0–11 scale) (mean)	6.8 (6.5 to 7.1)	7.2 (6.3 to 7.9)	6.7 (6.5 to 7.0)	0.4 (0 to 1.3)
No. of pain sites (median)	3.5 (3.3 to 3.8)	3.3 (2.7 to 4.1)	3.5 (3.3 to 3.8)	−1.0 (−1.5 to 1.5)
Location of pain (%) (4 most frequent sites)				
Head	67 (62 to 72)	63 (46 to 77)	67 (62 to 72)	−4 (−21 to 12)
Low back	45 (40 to 51)	46 (31 to 60)	45 (40 to 51)	1 (−17 to 19)
Abdomen	33 (28 to 37)	29 (14 to 43)	33 (27 to 40)	−5 (−21 to 11)
Chest	31 (26 to 37)	34 (17 to 51)	31 (26 to 36)	3 (−13 to 20)
Receiving pharmacotherapy for pain (%)	46 (41 to 52)	49 (31 to 66)	46 (40 to 52)	3 (−15 to 20)
Agents used for pain management, %‖				
Paracetamol	25 (21 to 30)	20 (9 to 34)	26 (21 to 31)	−6 (−2 to 10)
NSAIDS or aspirin	32 (27 to 37)	37 (20 to 54)	31 (26 to 37)	6 (−12 to 24)
Weak opioids¶	5 (3 to 7)	0 (0 to 0)	6 (3 to 9)	−6 (−8 to −3)
Alcohol	4 (2 to 6)	6 (0 to 14)	4 (2 to 6)	2 (−5 to 11)
Marijuana	3 (2 to 6)	3 (0 to 9)	4 (1 to 6)	−1 (−5 to 6)

*Rounding resulted in some percentages not adding to 100%.

†Sample size when there are missing data (whole cohort/HIV+/HIV−): age: n = 532/69/463; CD4 T-cell count$_{(\text{HIV+ only})}$: n = 65; HSCL-25: n = 530/70/460; female: n = 533/69/464; schooling: n = 521/70/451; employment: n = 532/70/462; pain the reason for being tested: n = 313/35/278.

‡Interval excludes 0.

§Full-time and part-time employed collapsed into single "employed" group.

‖Participants could be using more than on class of agent.

¶Codeine and tramadol.

HIV infection had not been diagnosed at the time, HIV-infected participants were not receiving antiretroviral therapy (ART) with their possible algogenic effects. However, participants who turned out to be HIV-uninfected were sufficiently concerned that they might be infected to have presented voluntarily for testing so did not have the level of peace of mind that members of a comparison group who knew they were HIV-uninfected might have; such peace of mind may well reduce anxiety and depression, and pain symptoms. The other novelty of our study was how different the South African context is compared with non-African countries. For example, although non-African cohorts of PLWH and pain have a high prevalence of substance use, the South African cohort here did not. Less than half of those with pain were receiving any pharmacotherapy at all, and the exposure to opioids, alcohol, and marijuana was 5% or less.

The frequency and extent of pain in the whole cohort was high, irrespective of HIV status, with 59% of the cohort having pain, on average of moderate to severe intensity, and a median of 3.5 pain sites per participant reporting pain. That frequency was in keeping with the frequency of pain in urban ambulatory HIV-infected cohorts in sub-Saharan Africa,[9,28,29] but well above the frequency in sub-Saharan African HIV-uninfected comparison cohorts.[30,31] Those comparison groups did not have the attributes of a proper control group, however. To the best of our knowledge, there are only 2 other published studies comparing pain frequency in which there was reasonable matching of attributes in groups of people

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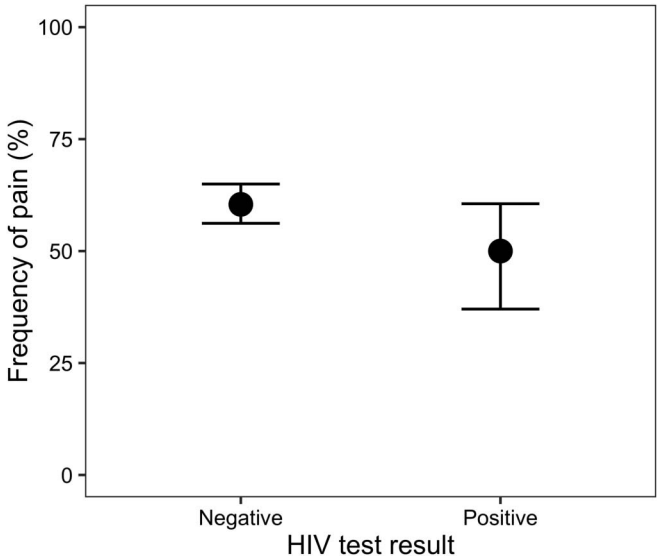

FIGURE 1. Frequency of pain in participants with (n = 70) and without (n = 465) an HIV infection. The point estimate and 95% CI of the difference in frequency were 10% and −2.0 to 24, respectively.

living with or without HIV.[32,33] PLWH in both cohorts had well-controlled HIV and >90% were on ART. One was a cohort study[32] conducted in the United Kingdom and Ireland, which included a comparison in pain frequency in 2 groups of people over 50 years of age, one in which the participants were uninfected and the other comprising individuals who were HIV-infected and well-controlled on ART; the groups were frequency-matched for age, sex, ethnicity, sexual orientation, and location (in or out of London). Pain frequency was marginally but significantly higher in the HIV-infected group, at 70%, than in the HIV-uninfected group, at 64%. The other study measured pain cross-sectionally during a prospective cohort study in American women with low socioeconomic status and HIV-risk behaviors including injection and illicit drug use.[33] HIV infection did not associate with presence of pain, and both HIV-positive and HIV-negative groups had a pain frequency of 50%. The notable difference between the 2 studies, other than geographical location and age range, was possible socioeconomic status and HIV-risk behavior. If education is used as a proxy for socioeconomic status,[34] two-thirds of the United Kingdom/Irish cohort had tertiary level education, compared with only a third in the American study, which was similar to the cohort here. HIV-risk behavior was not reported explicitly in the United Kingdom/Irish study. It is possible, therefore, lower socioeconomic status or HIV-risk behavior may rather associate with pain than HIV status. Unlike our study, neither of the studies assessed whether depression predicted pain.

Suggested causes for HIV-related pain include the algogenic effects of the HIV infection itself, pathological processes arising from immune dysregulation as a result of HIV infection, side effects of ART and adjunct therapies, and increased prevalence of depression and sleep disruption.[35,36] Indeed, depression and anxiety are associated with neuro-inflammation,[37] and are common risk factors for pain generally.[38] Our data demonstrated more severe depression and anxiety symptomatology to be associated with greater likelihood of pain in both univariate and multivariable analysis, with those participants with the highest scores on the HSCL-25 having a predicted probability of pain close to 100%. Pain and depression are frequently comorbid,[39] but this cross-sectional study was not designed to be able to determine the causative relationship between pain and depression, that is whether having pain led to depression, or depression to pain. However, our study did allow us to conclude that the very frequent pain in our cohort of potentially infected clients presenting at a VCT center was

TABLE 2. Results of Univariate Logistic Regression Models for the Presence of Pain

Predictors*	β (Odds Ratio)	β 95% CI (Odds Ratio)	Likelihood Ratio test†, χ^2	df	*P*
HIV status					
HIV Test results (positive)	−0.423 (0.655)	−0.929 to 0.082 (0.395–1.086)	2.699	1	0.100
Age					
Age	0.005 (1.005)	−0.011 to 0.021 (0.989–1.021)	0.390	1	0.532
Sex					
Sex (male)	−0.501 (0.606)	−0.850 to −0.153 (0.427–0.858)	7.988	1	0.005
Education					
Level of education (linear)	0.219 (1.245)	−0.400 to 0.828 (0.671–2.288)	1.178	2	0.555
Level of education (quadratic)	0.028 (1.029)	−0.366 to 0.427 (0.693–1.534)			
Employment					
Employment status (employed)	−0.747 (0.474)	−1.902 to 0.249 (0.149–1.282)	2.245	2	0.325
Employment status (unemployed)	−0.633 (0.531)	−1.786 to 0.360 (0.168–1.432)			
Depression and anxiety					
HSCL-25 total score	1.367 (3.927)	0.989 to 1.775 (2.688–5.901)	59.27	1	1.4e-14

*HIV status levels: positive/negative; sex levels: male/female; education levels (ordinal): grade 0–7/grade 8–12/>grade 12; employment levels: grant (pension, child, and disability)/employed (part-time or full time)/unemployed.
†Likelihood ratio test for the overall model.

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TABLE 3. Final Multivariable Model for the Presence of Pain*

Predictor	β (odds Ratio)	β 95% CI (Odds Ratio)	Wald Z	*P*
HSCL-25 total score	1.296 (3.654)	0.897 to 1.694 (2.452–5.443)	6.37	1.9e-10

*Selection by a backward elimination method.

associated far more with their depression and anxiety than with the presence or absence of the virus.

That HIV is not necessarily associated with a greater burden of pain contrasts with the paradigm that there is a greater prevalence of pain in cohorts with HIV compared with general populations,[1,2] and this additional burden may be related to the infection itself, secondary infective and noninfective diseases, and iatrogenic causes an increased burden of pain.[8] This finding that HIV is not necessarily associated with the development of pain is good news for individuals receiving a positive HIV diagnosis. Furthermore, this may help individuals overcome reluctance to test and assist in reducing stigma around HIV. That symptoms of depression- and anxiety-predicted pain indicates that assessment and treatment of mental health in the HIV testing and counseling setting may improve outcomes in all individuals. Furthermore, the presence of pain, depression, and anxiety reduces treatment adherence,[13,40,41] and so, such care could improve HIV outcomes too.

In our study, in addition to depression and anxiety symptomatology, female sex was associated with likelihood of having pain, on univariate analysis (but not multivariable modeling). While female sex is a recurring risk factor for pain in general populations,[42] whether it is a risk factor in populations of PLWH is equivocal,[35,43,44] possibly because it has been understudied. Other recurring risk factors for pain, such as increased age, and higher level of education,[2,45] were not associated with pain in our cohort on univariate or multivariable analysis (Tables 2 and 3). We conclude that, in our cohort, compared with depression and anxiety, increased age and lower level of education were not key risk factors for pain. The level of education was very similar within the group (most individuals had high school level of education: grades 8–12) and the homogeneity may have precluded us from identifying an association. The lack of a strong association with age is surprising, especially considering that ages ranged from less than 20 to more than 80 years. Being HIV-infected was not statistically significant in univariate analysis (Table 2) and nor was the variable retained in the multivariable model built by backward elimination (Table 3). Lower socioeconomic status, often associated with lower education and less employment,[34] frequently is associated with greater prevalence and intensity of pain.[45] Our participants lived in Soweto, a residential area encompassing much low cost and informal housing. Although there may have been a lack of heterogeneity in education, there was a range of individuals employed and unemployed, but state of employment was not associated with pain in any of our statistical analyses. It is possible that even those employed may have been in sufficient poverty for unemployment to have not featured as a risk factor for pain.

We investigated not just the likelihood of having pain but the sites at which pain occurred. Although the head and lower back are commonly the most prevalent pain sites in large pain cohorts, whether HIV-infected or not, the rate of headache in our study was 2–3 times higher than reported previously for ambulatory PLWH.[1,9,46] We are unsure of the reason for this discrepancy. A third of participants reported pain in the abdomen and/or chest. This rate of abdominal and chest pain is similar to that in an urban cohort of South Africans living with HIV,[9] but those sites did not rank in the top 11 most prevalent pain sites in a survey of 4000 Europeans with chronic pain.[1] Many clinicians working in sub-Saharan Africa believe that patients there show somatization of multiple ailments to the chest, and in the Cape Flats, a community similar to Soweto, there was documented somatization of depression as chest pain.[47] Indeed, a study of 3000 people from the Netherlands involved in a longitudinal study monitoring depression and anxiety found that 48% of participants had abdominal pain and 26% had chest pain, which was strongly associated with depression and anxiety.[48] Furthermore, somatization may be greater in countries, such as South Africa, where ongoing relationships between patient and physician, and thus rapport, are uncommon.[49]

There were further limitations to the study. Our study was completed at a single center in an urban area limiting the generalizability of the results to other populations, for example, rural populations. Also, our study was designed assuming that the frequency of pain in the HIV-infected group would be about 56%[9] and the frequency of pain in the uninfected group would be about 33%.[30] Thus, the study was not powered to detect small differences in frequency between the groups. The study would have been strengthened by having additional control groups. For example, a group of at-risk for HIV infection individuals not presenting for testing and a group not at risk of HIV infection were living in the same area. We did not record numbers of people declining to participate in the study, and so, we cannot comment on possible selection bias of who agreed to participate. Furthermore, because we did not record the date of any previous HIV test, it is possible that some individuals who tested HIV-uninfected may have been in the early preseroconversion stages of infection. However, because annual HIV incidence in South Africa was estimated as only 1.06%,[15] it is unlikely that this failure to detect infection would have had a significant effect on over-reporting of pain in the HIV-uninfected group. Previous cross-sectional studies have shown associations between HIV-risk factors and increased psychological distress,[50] and also between pain and increased HIV-risk behavior.[51] We did not assess the relationship between pain and psychological symptoms with HIV risk behaviors. It is possible that in this cohort of individuals seeking HIV testing that the high frequency of pain predicted increased HIV-risk behaviors. Conversely, we cannot be sure whether HIV-risk behaviors predicted an increased frequency of pain. Future studies of a longitudinal design would be required to determine these relationships. From a clinical point of view, associations between pain, psychological burden, and HIV-

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risk behaviors (regardless of the direction) further support the assessment and management of pain and mental health at HIV VCT centers.

In conclusion, we found that in a high HIV prevalence setting in South Africa, the overall frequency of pain in clients attending a VCT center, and assessed for pain before they knew their HIV status, was very high. Pain, however, did not depend on HIV status, or on education level and employment status. However, symptoms of depression and anxiety, which also were very prevalent, and being female sex were associated with likelihood of having pain. Our data do not exclude pain actually associated with the virus, or arising from algogenic effects of treatment, both of which may occur in PLWH for longer than our HIV-infected participants had been. However, our data, the first we believe to include data from properly-matched controls, did reveal a massive contribution to pain frequency in PLWH/AIDS from a high burden of pain in the populations from which they are drawn. This pain burden was associated particularly with a high burden of anxiety and depression. These data suggest that pain is not a necessary outcome of a positive HIV diagnosis, and such information could be disseminated in HIV education programs to reduce fear of testing for HIV.

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