HIV-related symptoms and management in HIV and antiretroviral therapy patients in KwaZulu-Natal, South Africa: A longitudinal study

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Abstract

Aim: The study aimed to determine the prevalence, predictors, and self-reported management of HIV- or ARV-related symptoms among HIV patients prior to antiretroviral therapy (ART) and over three time points while receiving ART in KwaZulu-Natal, South Africa. Method: A total of 735 consecutive patients (29.8% male and 70.2% female) who attended three HIV clinics completed assessments prior to ART initiation, 519 after 6 months, 557 after 12 months, and 499 after 20 months on ART. Results: The HIV patients reported an average of 7.5 symptoms (prior to ART), 1.2 symptoms after 6 months on ART, 0.3 symptoms after 12 months on ART, and 0.2 symptoms after 20 months on ART. The use of all management strategies decreased over the four different assessment periods from prior to ART to 20 months on ART. Conclusion: This study found a high symptom burden among HIV patients, which significantly decreased with progression on antiretroviral treatment. Several symptoms that persisted over time and several sociodemographic factors were identified that can guide symptom management. The utilisation of different symptom management strategies (medical, spiritual, complementary, and traditional) should be taken into consideration in HIV treatment.

Keywords: HIV symptoms, management strategies, antiretroviral therapy, longitudinal study

Résumé

Objectif. L’étude visait à déterminer la prévalence, les prédicteurs et la gestion, déclarée par les patients, des symptômes liés au VIH ou aux médicaments antirétroviraux avant la thérapie antirétrovirale (TAR) et à trois périodes déterminées au cours de la TAR. L’étude a eu lieu à KwaZulu-Natal, en Afrique du Sud. Méthode. Des patients ont fait l’objet d’évaluations dans trois cliniques du VIH. Des patients ont fait l’objet de stigmate intérieurisé, et qui consomment de l’alcool. Les symptômes les plus courants identifiés par le self-report incluent la tuberculose, diarrhée, maux de tête, les éruptions cutanées, la nausée, le vomissement et les douleurs, la neuropathie, le manque d’appétit, la toux, et les frissons. En général, les participants ont déclaré que les médicaments constituent la principale stratégie de gestion des symptômes, suivie de l’approche spirituelle. Les traitements complémentaires ou traditionnels arrivent au troisième rang. Toutes les stratégies de gestion ont connu une baisse au cours des quatre périodes d’évaluation, soit d’avant la TAR jusqu’à après 20 mois de TAR. Conclusion. Au cours de cette étude, il a été possible de conclure que les patients atteints de VIH doivent composer avec beaucoup de symptômes, et les symptômes diminuent au cours du traitement antirétroviral. Plusieurs symptômes persistants au fil du temps et plusieurs facteurs sociodémographiques ont été cernés. Ces facteurs pourront servir à guider la gestion des symptômes. L’utilisation de différentes stratégies de gestion des symptômes (médicale, spirituelle, complémentaire et traditionnelle) doit être prise en considération dans le cadre d’un traitement contre le VIH.

Mots clés: symptômes du VIH, stratégies de gestion, thérapie antirétrovirale, étude longitudinale

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Introduction
Few studies, especially longitudinal, have described the self-reported symptoms of people living with HIV (PLHIV) and antiretroviral therapy (ART) patients in sub-Saharan Africa (Bhengu, Ncama, McInerney, Wantland, Nicholas, Corless, et al. 2011; Friend-du Preez & Peltzer 2010; Makoe, Seboni, Molosiwa, Moleko, Human, Sukati, et al. 2005; Peltzer & Phaswana-Mafuya 2008; Wakeham, Harding, Bamukama, Levin, Kissa, Parkes-Ratanshi, et al. 2010), resulting in a paucity of evidence-based research on which to design appropriate interventions. ‘HIV/AIDS symptoms can result from the disease itself, from secondary complications of the disease, or from side effects of highly active ART (HAART) and other medications related to comorbidities. HIV symptoms are the single most important indicators for patients and practitioners. Symptoms prompt patients to seek medical attention and provide health care providers with essential clues about changes in health status and quality of life’ (Portillo, Holzemer & Chou 2007:1824). This study describes the symptom experiences of PLHIV about to commence ART and at three time points over 20 months on ART who were residing in resource-poor communities in KwaZulu-Natal, South Africa. The relationship between current symptoms and management strategies in this setting is also investigated.

It is estimated that approximately 5.6 million people are living with HIV and AIDS and 1.7 million were on ART in South Africa in 2012, more than in any other country (UNAIDS 2012). The highest prevalence (24.7% in the general population) is found in the province of KwaZulu-Natal (National Department of Health 2012). Rollout of ART began in 2004 and the number of people enrolled (1.7 million) is now the highest in the world (UNAIDS 2012). Although as people begin treatment, they can expect to live longer, most patients initiate HAART at advanced stages of the disease with very low CD4 counts and in poor health (May, Boulle, Phiri, Messou, Myer, Wood, et al. 2010). In the Southern African context and in other studies, a higher symptom frequency has been reported by those in advanced stages of the disease (patients who have recently been hospitalised, been given an AIDS diagnosis, and those with lower CD4 counts), patients of lower socio-economic status (Gonzalez, Penedo, Labre, Durán, Antoni, Schneiderman, et al. 2007; Harding, Lampe, Norwood, Date, Cucas, Fisher, et al. 2010; Makoae et al. 2005; Peltzer & Phaswana-Mafuya 2008), those on ART (Harding, Molloy, Easterbrook, Frame & Higginson 2006), and those with a poor ART adherence (Gonzalez et al. 2007; Harding et al. 2010).

The study aimed to determine prevalence, predictors, and self-reported management of HIV- or ARV-related symptoms among HIV patients prior to ART and over three time points while receiving ART in KwaZulu-Natal, South Africa.

Methods
Sampling and procedure
This is a prospective study of all treatment-naïve patients (N = 735) recruited from the three public hospitals in the Uthukela health district in KwaZulu-Natal from October 2007 to February 2008. All ARV-naïve patients who were about to commence ARVs (18 years and above) and who consecutively attended the HIV clinics during the recruitment period were eligible for this study. Systematic sampling was used by asking health care providers for referrals of ART-naïve patients (eligible for ARV treatment but who had not commenced ARV treatment yet). Physicians from the three selected public clinics asked every consecutively visiting ART-naïve patient meeting the inclusion criteria of being 18 years or over if they would like to complete a confidential survey and interview concerning their health and social situation. This would include information from their medical records on details of their medical condition, laboratory tests, and treatment. It was made clear to patients that their participation in this study was voluntary and that a decision not to participate would not affect their medical care. If the potential participant indicated an interest in participating, the health care provider then referred them to an external Human Sciences Research Council research assistant. The ART-naïve patients were then asked to sign and complete a consent form before the interview took place in a private area in or outside the clinic. The interviews were conducted by four trained external HSRC researchers (one or two per HIV clinic) in interviewer-administered semi-structured interviews. Permission to access patient medical records was sought from both the patient and the health worker/manager. Questionnaires were anonymised, with no personal identifying information recorded on them. Recruitment took place over a period of four months, with a 97.8% participation rate. Data were collected using an interviewer-administered semi-structured questionnaire.

The questionnaire was translated into the major language spoken in the study area (Zulu) and verified by a second translator. Where inconsistencies were found, these were corrected (Peltzer, Friend-du Preez, Ramlagan & Fomundam 2008). The patients were then interviewed again at the 6, 12, and 20 months clinic visits post-initiation of ART. Patients who did not attend the planned follow-up were contacted by telephone and up to two home visits before being considered lost to follow-up. Sample size calculations using Epi Info Version 7.1 found that based on the expected frequency of patients who would have symptoms of 25% (based on Makoae et al. 2005, confidence limit 5%, three clusters of study, a confident level of 99% yielded a cluster size of 166), a total of 498 was chosen as the minimum sample size. The study protocol was approved by the Human Sciences Research Council ethics committee, the KwaZulu-Natal Department of Health, the Uthukela Health District and the three superintendents of the three study hospitals.

Measures
The patients were interviewed with an anonymous questionnaire that requests information on sociodemographic characteristics, clinical history, and health-related characteristics and health beliefs. Clinical data relating to date of HIV diagnosis, HIV acquisition and transmission risk factors, current CD4 cell count, and viral load were obtained from the medical chart.

The revised signs and symptoms checklist for persons with HIV disease
The SSC-HIVrev is a 72-item checklist of HIV/AIDS-specific physical and psychological symptoms scored using the following
scale: 0 = not checked (not present today), 1 = mild, 2 = moderate, and 3 = severe (Holzemer, Hudson, Kirksey, Hamilton & Bakken 2001). The validity and reliability of the instrument have previously been reported for a US sample (Holzemer et al. 2001) and various African countries (Makoae et al. 2005), including South Africa (Peltzer & Phaswana-Mafuya 2008); the reliability estimates ranged from 0.76 to 0.94. The Cronbach α reliability coefficient of this 64-item scale was 0.95 at baseline and 0.84, 0.95, and 0.78 for the three subsequent assessment periods, indicating the excellent internal consistency reliability of the items. The presence of any symptom was added up to form the total HIV-related symptom burden.

Self-reported HIV-related symptoms and management
Participants were asked to describe three to six HIV- and/or ARV-related symptoms they had experienced, list the strategies (medications, complementary or traditional treatments, self-comforting, changing diet, seeking help, exercise, spiritual care, and daily thoughts/activities to make themselves feel better) they used to manage these symptoms, and rate the perceived effectiveness of these strategies (Sukati, Msdebele, Makoa, Ramukumba, Makoae, Seboni, et al. 2005).

Internalised AIDS stigma
We used the six-item internalised AIDS-related stigma scale for people infected with HIV (Kalichman, Simbayi, Cloete, Mthembu, Mkbona & Ginindza 2009b). Items reflected self-defacing beliefs and negative perceptions of PLHIV/AIDS. For example, ‘It is difficult to tell other people about my HIV infection’. Response options ranged from 1 = strongly agree to 4 = strongly disagree. The Cronbach α reliability coefficient of this six-item scale was 0.80 at baseline and 0.64, 0.66, and 0.78 for the three subsequent assessment periods, indicating the excellent to moderate internal consistency reliability of the items.

HIV/AIDS discrimination experiences
To assess AIDS-related discrimination, we asked participants whether they had experienced seven discrimination-related events, e.g. whether they had been treated differently since they had disclosed their HIV status to friends and family; whether being HIV positive had caused them to lose a job or a place to stay; and whether they had experienced discrimination because they are HIV positive (Simbayi, Kalichman, Strebel, Cloete, Mthembu, Mkhonta & Ginindza 2009b). Because AUDIT-C is reported to be less sensitive at identifying risk drinking in women, the cut-off points for binge drinking for women were reduced by one unit compared with men (Freeborn, Polen, Hollis & Senft 2000). Gual, Segura, Contel, Heather and Colon (2002) recommend a cut-off point of ≥ 5 for men and ≥ 4 for women; despite this, the false positive rate was 46.5% among male and 63.3% among female patients when compared with a clinical diagnosis of risky drinking. Cronbach’s alpha for the AUDIT-C in this sample was 0.91 at Time 4.

Alcohol use disorder
The alcohol use disorders identification test (AUDIT-C) focuses solely upon the consumption of alcohol (i.e. the frequency of drinking, the quantity consumed at a typical occasion, and the frequency of heavy episodic drinking (i.e. consumption of six standard drinks or more on a single occasion – in South Africa, a standard drink is 12 g alcohol)) (Babor, Higgins-Biddle, Saunders & Monteiro 2001). The validity and reliability of the instrument have previously been reported for a US sample (Holzemer et al. 2001) and various African countries (Makoae et al. 2005), including South Africa (Peltzer & Phaswana-Mafuya 2008); the reliability estimates ranged from 0.76 to 0.94. The Cronbach α reliability coefficient of this 64-item scale was 0.95 at baseline and 0.84, 0.95, and 0.78 for the three subsequent assessment periods, indicating the excellent internal consistency reliability of the items. The presence of any symptom was added up to form the total HIV-related symptom burden.

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Data analysis
Data were analysed using Statistical Package for the Social Sciences for Windows software application programme version 17.0. Frequencies, means, standard deviations, median, and inter-quartile ranges were calculated to describe the sample. To identify the pattern of factors characterising the HIV-related symptom burden at any assessment, linear regression models based on generalised estimating equations (GEEs) were used. These models allowed for the consideration of the correlation among within-subject repeated measures (Twisk 1997). For the univariate analyses, simple linear regression was used to identify factors associated with the HIV-related symptom burden; variables with p-values lower than 0.05 were entered in the corresponding multiple regression model. A forward procedure based on the quasi likelihood ratio test produced the final model.

Results
A total of 735 patients (217 men and 518 women) completed a baseline questionnaire at Time 1 prior to initiating ART. Follow-up questionnaires were completed at the 6-month follow-up by 519 patients within this cohort (139 men and 370 women) who had now been on ART for 6 months, 12 months later by 557 patients within this cohort (157 men and 396 women), and 20 months later by 499 patients (126 men and 333 women) and 236 (32.1%) participants were lost to follow-up (including transfers): 83 (11.3%) were known to have died, 74 (10.1%) transferred care elsewhere, 14 (1.9%) refused participation, 12 (1.6%) were not initiated on ART, and 53 (7.2%) could not be traced. At Time 4, the HIV medications for 380 (76.3%) patients were Lamivudine (3TC), Stavudine (d4T) + Efavirenz and for 118 (23.7%) patients were Lamivudine (3TC), Stavudine (d4T) + Nevirapine.

Sample characteristics
The mean age of the participants at baseline assessment was 35.9 years (SD = 9.7) and the educational level of the majority (81.0%) was less than Grade 12. Almost three-quarters (71.8%) had never married, 61.2% were unemployed and 20.2% employed, more than half (52.3%) had a child care grant, 29.9% had a formal salary, and 7.9% had no income. Almost two-thirds (63.3%) resided in a rural area, most (73.5%) had
recently been (within the past year) diagnosed as being HIV positive, and almost all (96.1%) had disclosed their HIV status to someone. While baseline characteristics were similar between men and women, women were more likely to be younger and receiving social (including child care) grants and men were more likely to be married or cohabiting, employed, and have a formal salary. The median CD4 count at the 20-month follow-up was 446 cells/cu.mm compared with 261 cells/cu.mm at the 12-month follow-up, 130 cells/cu.mm at the 6-month follow-up, and 119 cells/cu.mm prior to ARV initiation. A study attrition analysis comparing participants who left the study with those who stayed found significant differences in terms of a lower educational level, rural residence, employment status (which is most likely a function of increased mobility for more educated individuals who can find work in urban areas), and lower HIV symptoms for those who stayed in the study and no significant differences in terms of gender, age, religion, income, time since HIV diagnosis, CD4 cell counts, internalised stigma, discrimination experience, and alcohol use (see Table 1).

**Table 1. Sample characteristics and study attrition analysis.**

| Variable                  | Baseline (Time 1) | Stayed in the study (Time 4) |
|---------------------------|-------------------|------------------------------|
| N                          | 735 or M | % or SD | 499 or M | % or SD | χ² or t-test | p  |
| Sex                       | Male    | 217     | 29.5    | 137     | 63.1    | 3.2    | 0.07    |
|                           | Female  | 518     | 70.5    | 362     | 69.9    |        |         |
| Age, range 18–67          |         | 35.9    | 9.7     | 36.1    | 9.5     | -0.82  | 0.42    |
| Education                 | Grade 7 or less | 279      | 38.1    | 199     | 71.3    | 4.39   | 0.04    |
|                           | Grade 8–11 | 314      | 42.9    | 214     | 68.2    | 0.02   | 0.9     |
|                           | Grade 12 or more | 139     | 19.0    | 84      | 60.4    | 4.39   | 0.04    |
| Religion                  | African or none | 88      | 25.4    | 121     | 64.7    | 1.17   | 0.28    |
|                           | Mainstream Christian | 154  | 21.0    | 99      | 64.3    | 1.17   | 0.28    |
|                           | Charismatic | 271     | 36.9    | 194     | 71.6    | 2.69   | 0.1     |
| Residence                 | Rural (village) | 338     | 46.2    | 215     | 63.6    | 5.19   | 0.02    |
|                           | Rural (farm) | 125     | 17.1    | 95      | 76      | 4.59   | 0.03    |
|                           | Urban (informal settlements) | 41  | 5.6     | 32      | 78      | 2.07   | 0.15    |
|                           | Urban (formal settlements) | 227   | 31.1    | 154     | 67.8    | 0      | 1       |
| Employment status         | Housewife/ houseman | 99     | 13.5    | 74      | 74.7    | 2.37   | 0.12    |
|                           | Unemployed | 448     | 61.2    | 290     | 64.7    | 5.78   | 0.02    |
|                           | Employed    | 148     | 20.2    | 110     | 74.3    | 3.38   | 0.07    |
|                           | Pensioner/ disabled/ student | 24  | 3.4     | 14      | 56      | 1.72   | 0.19    |
| Income                    | Formal salary | 215     | 29.9    | 157     | 73      | 2.94   | 0.09    |
|                           | Family member contributions | 133   | 18.5    | 89      | 66.9    | 0.18   | 0.67    |
|                           | Social grants | 264     | 36.7    | 182     | 68.9    | 0.04   | 0.84    |
|                           | Disability grant (for chronic illness) | 129   | 23.8    | 89      | 69      | 0.27   | 0.61    |
|                           | Child care support grant | 383  | 52.3    | 262     | 68.4    | 0.13   | 0.71    |
|                           | No income | 57      | 7.9     | 38      | 63.2    | 0.81   | 0.37    |
| Time since HIV diagnosis  | ≤1 year (2007/8) | 540      | 73.5    | 367     | 68      | 0.01   | 0.95    |
|                           | 1–2 years (2006) | 73       | 9.9     | 55      | 75.3    | 2.06   | 0.15    |
|                           | >2 years (2005–1995) | 122    | 16.6    | 77      | 63.1    | 1.53   | 0.22    |

(Continued)

**Table 1. Continued.**

| Variable                  | Baseline (Time 1) | Stayed in the study (Time 4) |
|---------------------------|-------------------|------------------------------|
| N                          | 735 or M | % or SD | 499 or M | % or SD | χ² or t-test | p  |
| CD4 count (cells/μL)      | 1–99    | 106     | 19.7    | 91      | 85.8    | 0.2    | 0.66    |
|                           | 100–349 | 345     | 64.2    | 300     | 87      | 0.03   | 0.86    |
|                           | ≥350    | 86      | 16.1    | 77      | 89.5    | 0.52   | 0.47    |
| The number of HIV symptoms | (range: 0–64) | 7.2     | 9.5     | 6.8     | 9.3     | 2.64   | 0.008   |
| Internalised stigma       | (range: 0–6) | 3.8     | 2.4     | 4.2     | 2.7     | -0.99  | 0.32    |
| Discrimination experiences | (range: 0–7) | 0.3     | 1.0     | 0.3     | 0.6     | 0.5    | 6.7     |
| AUDIT scores              | (range: 0–12) | 0.4     | 1.4     | 0.6     | 1.3     | -0.78  | 0.43    |

HIV-related symptom changes over 20 months of follow-up

The baseline mean total score on the HIV-symptom scale for the 735 patients was 7.5 (SD = 9.6), which significantly decreased at Time 2–1.2 (SD = 2.6), at Time 3–0.3 (SD = 2.1), and at Time 4–0.2 (SD = 0.9) (F = 2193.69; p < 0.001). An examination of individual HIV-symptom items indicated that the percentage of patients scoring mild, moderate, or severe (defined as a score of 1 or more) decreased over time for all items. The most obvious change was for ‘concerned over weight loss’ and ‘dry mouth’; approximately one-third (35.7% and 31.7%) of patients scored ‘yes’ on these items at baseline, but none
scored ‘yes’ at the 20-month follow-up. The five most frequently reported symptoms at Time 1 were concern over weight loss, headaches, dry mouth, memory loss, and weakness; at Time 2, chills, headaches, diarrhoea, concern over weight gain, and dry mouth; at Time 3, headaches, diarrhoea, numbness/tingling of legs, lack of appetite, and painful joints; and at Time 4, painful joints, diarrhoea, lack of appetite, fever, and headaches. The scores for each HIV-symptom item at each of the four assessments are given in Table 2.

Predictors of HIV-related symptom burden
To identify at any assessment the pattern of factors characterising the HIV-related symptom burden (all symptoms together), linear regression models based on generalised estimating equations (GEEs) were used. When univariate analyses were employed and in the GEE multiple regression model (see Table 3), not being employed, lower CD4 cell counts, internalised stigma, and alcohol use were associated with a greater HIV-related symptom burden. Furthermore, in a separate model, ART adherence (from Times 2 to 4) was not found to be associated with the HIV-related symptom burden (from Times 2 to 4) ($\beta$ coefficient 0.06 (95% CI: −0.04 to 0.201) ($p = 0.091$).

HIV- or ARV-related self-reported symptoms and management
Participants first listed 3–6 HIV- or ARV-related symptoms. The five most common symptoms or conditions identified at Time 1 (prior to ART) were tuberculosis, headaches, diarrhoea, weight loss, and cough; at Time 2, headaches, diarrhoea, rash, nausea and vomiting, and pains; at Time 3, headaches, numbness/tingling, pains, rash, and lack of appetite; and at Time 4, diarrhoea, rash, headaches, chills, and pains (see Table 4).

Regarding management strategies for the self-reported HIV- or ARV-related symptoms, medications were the most frequently mentioned care strategies and ranked first in overall use, ranging from 22.5% at Time 3 to 85.9% at Time 2. This was followed by spiritual care at 33.3% at Time 1 and at 46.4% at Time 2 and complementary or traditional treatments at 37% at Time 1 and at 30.9% at Time 2. Overall, all different management strategies decreased over the four different assessment periods from prior to ART to 20 months on ART (see Table 5).

Discussion
In this study, HIV patients reported an average of 7.5 symptoms (prior to ART), 1.2 symptoms after 6 months on ART, 0.3 symptoms after 12 months on ART, and 0.2 symptoms after 20 months on ART on the day of the interview, with a higher symptom frequency amongst patients who were not employed, experienced internalised stigma, used alcohol, and had lower CD4 cell counts. The duration of HIV diagnosis was not associated with the HIV-related symptom burden. Other studies (Gonzalez et al. 2007; Makoe et al. 2005) also found that lower CD4 cell counts were associated with higher HIV-related symptoms. As found in other studies (Gonzalez et al. 2007; Harding et al. 2010; Makoe et al. 2005; Peltzer & Phaswana-Mafuya 2008), this study found that lower socio-economic status or not being employed was associated with the HIV-related symptom burden. This study did not find that poor ART adherence was associated with HIV-related symptoms, which was also found in a study in KwaZulu-Natal, South Africa (Bhengu et al. 2011), but some other studies (Gonzalez et al. 2007; Harding et al. 2010) found an association between poor ART adherence and HIV-related symptoms.

The five most frequently reported symptoms on the structured questionnaire at Time 1 were concern over weight loss, headaches, dry mouth, memory loss, and weakness; at Time 2, chills, headaches, diarrhoea, concern over weight gain, and dry mouth; at Time 3, headaches, diarrhoea, numbness/tingling of the legs, lack of appetite, and painful joints; and at Time 4, painful joints, diarrhoea, lack of appetite, fever, and headaches. In an open-ended question, the most common symptoms or conditions identified included tuberculosis, diarrhoea, headaches, rash, nausea and vomiting, and pains. Similar symptoms have been reported from other studies in Southern Africa (Bhengu et al. 2011; Makoe et al. 2005; Peltzer & Phaswana-Mafuya 2008). It is interesting to note that diarrhoea and pain, including headache and numbness/neuropathy, were frequently mentioned across the different assessment periods in this study, as also found in other studies (Bhengu et al. 2011; Sukati et al. 2005; Tsai, Hsiung & Holzemer 2002). This suggests that the management of pain and peripheral neuropathy should be prioritised by clinicians providing HIV/AIDS care (Bhengu et al. 2011; Nicholas, Voss, Wantland, Lindgren, Huang, Holzemer, et al. 2010). Harding, Simms, Alexander, Collins, Combo and Memiah (2013) showed the evidence that integrated HIV outpatient palliative care in the presence of ART can ameliorate the high burden of pain, symptoms, and other multidimensional problems that persist alongside HIV treatment.

Overall, the participants reported medications as the most frequently occurring management strategy and the most effective, second was spiritual care, and third was complementary or traditional treatments. This finding suggests that participants in this study used their medical provider as a major source of the management of their symptoms. Furthermore, spiritual, complementary, or traditional treatments apparently play an important role in PLHIV. All types of management strategies decreased over the four different assessment periods from prior to ART to 20 months on ART. In a different study in Southern Africa using the same management categories, medications were also ranked first, complementary treatments were ranked second, and spiritual care was ranked seventh (Sukati et al. 2005). In terms of traditional and complementary treatments in this sample, the use of herbal therapies for HIV declined significantly from 36.6% prior to ART to 8.0% after 6 months, 4.1% after 12 months, and 0.6% after 20 months on ARVs. Faith healing methods (including spiritual practices and prayer) declined from 35.8% to 22.1%, 20.8%, and 15.5%, respectively (Peltzer, Fried-du Preez, Ramlogan, Fonumdam, Anderson & Chanetsa 2011). The use of different symptom management strategies should be taken into consideration in HIV treatment.

Limitations
Viral load data were only available for a few participants and so this category was therefore excluded from the analysis.
| Problem                                    | Time 1 | Rank | Time 2 | Rank | Time 3 | Rank | Time 4 | Rank |
|--------------------------------------------|--------|------|--------|------|--------|------|--------|------|
| 1. Concern over weight loss                | 35.7   | 1    | 1.5    | 29   | 0.4    | 22   | 0      |      |
| 2. Headaches                               | 32.1   | 2    | 6.3    | 2    | 2.5    | 1    | 1.2    | 5    |
| 3. Dry mouth                               | 31.7   | 3    | 4.0    | 5    | 0.5    | 12   | 0      |      |
| 4. Memory loss                             | 27.0   | 4    | 3.8    | 6    | 0.4    | 23   | 0      |      |
| 5. Weakness                                | 24.8   | 5    | 3.4    | 8    | 0.5    | 13   | 0      |      |
| 6. Thirsty                                 | 24.2   | 6    | 2.9    | 14   | 0      | 0    |        |      |
| 7. Painful joints                          | 23.6   | 7    | 3.8    | 7    | 1.3    | 5    | 1.8    | 1    |
| 8. Chills (feeling very cold)              | 23.1   | 8    | 9.9    | 1    | 0.9    | 8    | 0.2    | 15   |
| 9. Chest pain                              | 22.9   | 9    | 3.1    | 11   | 1.3    | 6    | 0.2    | 16   |
| 10. Numbness/tingling of legs              | 21.3   | 10   | 3.1    | 12   | 1.4    | 3    | 0      |      |
| 11. Lack of appetite                       | 20.9   | 11   | 2.7    | 6    | 1.4    | 4    | 1.4    | 3    |
| 12. Diarrhoea                              | 20.3   | 12   | 5.4    | 3    | 2.0    | 2    | 1.6    | 2    |
| 13. Numbness/tingling of feet/ toes        | 20.3   | 13   | 2.3    | 21   | 0.4    | 24   | 0      |      |
| 14. Heart racing                           | 17.5   | 14   | 1.1    | 35   | 0.2    | 41   | 0      |      |
| 15. Fatigue                                | 17.4   | 15   | 1.9    | 24   | 0.2    | 42   | 0      |      |
| 16. White spots in mouth/thrush            | 17.3   | 16   | 1.3    | 30   | 0.5    | 14   | 0.4    | 11   |
| 17. Numbness/tingling of hands/fingers     | 17.1   | 17   | 2.9    | 15   | 0.4    | 25   | 0      |      |
| 18. Night sweats                           | 16.3   | 18   | 2.3    | 22   | 0      | 0.2   | 17     |      |
| 19. Dizziness                              | 15.6   | 19   | 3.4    | 9    | 0.4    | 26   | 1.2    | 6    |
| 20. Muscle aches                           | 15.0   | 20   | 1.3    | 31   | 0.4    | 27   | 0.2    | 18   |
| 21. Depression (sadness)                   | 14.8   | 21   | 2.5    | 19   | 0.5    | 15   | 0      |      |
| 22. Fear/worry                             | 14.3   | 22   | 2.5    | 20   | 0.4    | 28   | 0      |      |
| 23. Nausea                                 | 14.1   | 23   | 2.7    | 17   | 0.4    | 29   | 0      |      |
| 24. Rash                                   | 13.8   | 24   | 2.7    | 18   | 0.5    | 16   | 0.4    | 12   |
| 25. Numbness/tingling of arms              | 13.1   | 25   | 1.7    | 27   | 0      | 0    |        |      |
| 26. Day sweats                             | 12.8   | 26   | 2.1    | 23   | 0.2    | 43   | 0      |      |
| 27. Difficulty concentrating              | 12.0   | 27   | 1.1    | 36   | 0.4    | 30   | 0      |      |
| 28. Abdominal pain                         | 11.9   | 28   | 1.3    | 32   | 0.5    | 17   | 0.8    | 9    |
| 29. Insomnia/cannot sleep                  | 11.6   | 29   | 0.6    | 49   | 0      | 0    |        |      |
| 30. Hump on back of neck/shoulders         | 11.6   | 30   | 1.1    | 37   | 0.4    | 31   | 0      |      |
| 31. Vomiting                               | 11.5   | 31   | 1.0    | 41   | 0.7    | 11   | 0      |      |
| 32. Loose stools                           | 10.9   | 32   | 1.9    | 25   | 0.4    | 32   | 0.2    | 19   |
| 33. Coughing/problems catching breath      | 10.5   | 33   | 0.8    | 43   | 0.9    | 9    | 1.2    | 7    |
| 34. Fever                                  | 10.0   | 34   | 3.4    | 10   | 1.1    | 7    | 1.4    | 4    |
| 35. Easy bruising                          | 9.4    | 35   | 0.4    | 54   | 0      | 0.2   | 20     |      |
| 36. Itchy skin                             | 9.3    | 36   | 1.3    | 33   | 0.9    | 10   | 0.6    | 10   |
| 37. Concern over weight gain               | 8.6    | 37   | 4.6    | 4    | 0.5    | 18   | 0      |      |
| 38. Anxious                                | 8.5    | 38   | 0.4    | 55   | 0.2    | 44   | 0      |      |
| 39. Burning with urination                 | 8.3    | 39   | 0.8    | 44   | 0.4    | 33   | 0.2    | 21   |
| 40. Shortness of breath at rest            | 7.9    | 40   | 0.4    | 56   | 0      | 55   | 0      |      |
| 41. Shortness of breath with activity      | 7.4    | 41   | 0.6    | 50   | 0.2    | 45   | 0      |      |
| 42. Weight gain in stomach area            | 7.4    | 42   | 1.7    | 28   | 0.5    | 19   | 0.2    | 22   |
| 43. Swollen feet                           | 7.0    | 43   | 1.1    | 38   | 0.4    | 34   | 0.4    | 13   |
| 44. Skinny arms and legs                   | 6.7    | 44   | 0.8    | 45   | 0.2    | 46   | 0      |      |
| 45. Rectal discharge                       | 6.7    | 45   | 1.1    | 39   | 0.4    | 35   | 0      |      |
| 46. Mouth ulcers                           | 6.6    | 46   | 0.2    | 61   | 0.2    | 47   | 0      |      |

(Continued)

Table 2. Symptom frequency (mild, moderate, or severe) in percentage over time.
Furthermore, the assessment of ART adherence and other measures was relied on the self-report. The study results may be biased in favour of those who survived and were healthy enough to participate in follow-up. Sample attrition is a methodological artefact that can potentially influence longitudinal studies (Burgoyne, Rourke, Behrens & Salit 2004). The symptoms

### Table 2. Continued.

| Problem                  | Time 1 | Rank | Time 2 | Rank | Time 3 | Rank | Time 4 | Rank |
|--------------------------|--------|------|--------|------|--------|------|--------|------|
| 47. Wheezing             | 6.0    | 47   | 0.6    | 51   | 0.2    | 48   | 0      |
| 48. Seizures/tremors     | 6.0    | 48   | 1.1    | 40   | 0      | 0    |
| 49. Constipation         | 5.8    | 49   | 0.2    | 62   | 0.4    | 36   | 0.2    | 23   |
| 50. Blurred vision       | 5.7    | 50   | 2.1    | 24   | 0.4    | 37   | 0      |
| 51. Sore throat          | 5.6    | 51   | 0.2    | 63   | 0.5    | 20   | 0.2    | 24   |
| 52. Rectal itching       | 5.5    | 52   | 0.8    | 46   | 0      | 0    |
| 53. Gas/bloating         | 5.2    | 53   | 3.1    | 13   | 0.5    | 21   | 0      |
| 54. Painful swallowing   | 5.2    | 54   | 0      | 64   | 0.4    | 38   | 0      |
| 55. Nipple discharge     | 5.2    | 55   | 0.8    | 47   | 0      | 0    | 0.2    | 25   |
| 56. Rectal bleeding      | 4.9    | 56   | 1.3    | 35   | 0      | 0    |
| 57. Swollen glands       | 4.8    | 57   | 0.4    | 57   | 0      | 1.2  | 8      |
| 58. Prominent leg veins  | 4.4    | 58   | 1.0    | 42   | 0.4    | 39   | 0      |
| 59. Flushing             | 4.2    | 59   | 0.4    | 58   | 0      | 0    | 0.4    | 14   |
| 60. Sore/bleeding gums   | 3.8    | 60   | 0.8    | 48   | 0      | 0    |
| 61. Breast pain/changes  | 3.7    | 61   | 0.4    | 59   | 0.4    | 40   | 0.2    | 26   |
| 62. Sore/or lumps on genitals | 3.7 | 62 | 0.6 | 52 | 0 | 0.2 | 27 |
| 63. Blood in spit/sputum | 3.4    | 63   | 0.4    | 60   | 0.2    | 49   | 0.2    | 28   |
| 64. Nose bleeds           | 2.6    | 64   | 0.6    | 53   | 0      | 0    | 0.2    | 29   |
| Total mean (SD)           | 7.5 (9.6) | 1.2 (2.6) | 0.3 (2.1) | 0.2 (0.9) |

### Table 3. Predictors of the HIV-related symptom burden.

| Variables                          | $\beta$ coefficient (95% CI) | $p$   | Adjusted $\beta$ coefficient (95% CI)* | $p$ |
|------------------------------------|------------------------------|------|----------------------------------------|-----|
| Sociodemographic variables         |                              |      |                                        |     |
| Age                                | 0.01 (–0.004, 0.014)          | 0.307| –                                      |     |
| Male vs. female                    | 0.05 (–0.14, 0.25)            | 0.589| –                                      |     |
| Educational level                  | 0.05 (0.01, 0.09)             | 0.014| 0.12 (–0.01,0.24)                      | 0.05|
| Never married/widowed/separated/divorced vs. married or cohabiting | 0.05 (–0.14, –0.25) | 0.602| –                                      |     |
| Urban vs. rural residence           | –0.77 (–0.95, –0.59)          | <0.001| 0.24 (–0.33, 0.81)                     | 0.406|
| Formal/informal employment vs. not | –1.03 (–1.23, –0.84)          | <0.001| –2.36 (–3.00, –1.72)                   | <0.001|
| Clinical variables                 |                              |      |                                        |     |
| Time since HIV diagnosis           | –0.09 (–0.21, 0.03)           | 0.147| –                                      |     |
| CD4 count (cells/µL)               | –3.41 (–5.44, –1.39)          | 0.001| –0.01 (–0.011, –0.017)                 | <0.001|
| Social variables                   |                              |      |                                        |     |
| Internalised stigma scores         | 0.54 (0.49, 0.59)             | <0.001| 0.66 (0.57, 0.76)                      | <0.001|
| Discrimination experiences score   | –0.31 (–0.44, –0.17)          | <0.001| 0.25 (–0.14, 0.64)                     | 0.204|
| Alcohol use score                  | 0.24 (0.07, 0.42)             | 0.007| 0.33 (0.14,0.51)                      | <0.001|

Note: All variables with $p<.05$ in the baseline HIV-related symptom burden adjusted model were eligible for the multivariate model.

*Goodness of fit quasi-likelihood under independence model criterion value $= 44,318.46$. 
described by participants may represent symptoms of HIV disease, side effects of antiretroviral treatment, or a combination of both effects of medications and HIV disease (Bhengu et al. 2011). Finally, the findings are derived from a sample of men and women residing in one district in one province in South Africa. Thus, caution is urged in generalising the findings to other districts and provinces in the country.

### Table 4. HIV- or ARV-related self-reported symptoms.

| Symptom                              | Time 1 | Time 2 | Time 3 | Time 4 |
|--------------------------------------|--------|--------|--------|--------|
|                                      | N      | Rank order | N    | Rank order | N    | Rank order | N    | Rank order |
| Headaches                            | 56     | 2       | 83    | 1       | 38    | 1       | 8    | 3         |
| Diarrhoea                            | 48     | 3       | 51    | 2       | 17    | 3       | 97   | 1         |
| Rash                                 | 25     | 8       | 45    | 3       | 15    | 4       | 10   | 2         |
| Nausea and vomiting                  | 25     | 8       | 41    | 4       | 11    | 6       | 1    | 9         |
| Numbness/tingling of legs/arms/hands/feet (neuropathy) | 17 | 13      | 21    | 5       | 23    | 2       | 1    | 9         |
| Pain (chest, leg, body)              | 24     | 9       | 20    | 6       | 17    | 3       | 5    | 5         |
| Lack of appetite                     | 26     | 7       | 11    | 7       | 13    | 5       | 4    | 6         |
| Fatigue                              | 22     | 11      | 6     | 9       | 2     | 10      | 1    | 9         |
| Tuberculosis                         | 175    | 1       | 1     | 11      | 2     | 8       |      |           |
| Herpes                               | 26     | 38      | 2     |         |       |         |      |           |
| Stomach problem                      | 19     | 12      | 5     | 10      | 7     | 7       | 3    | 7         |
| Thrush                               | 17     | 13      | 5     | 10      |       |         |      |           |
| Chills (feeling very cold)           |        |         | 5     | 8       | 6     | 4       |      |           |
| Weight loss                          | 39     | 4       |       |         |       |         |      |           |
| Cough                                | 33     | 5       | 9     | 8       |       |         |      |           |
| Discharge disorder; STI               | 28     | 6       | 2     | 12      | 3     | 9       |      |           |
| Memory loss                          |         | 9       | 8     | 7       | 7     |         |      |           |
| Night sweats                         | 5      | 16      | 5     | 10      |       |         |      |           |
| Itchy skin                           | 7      | 14      | 2     | 12      |       |         |      |           |
| Swollen glands                       | 6      | 15      |       |         |       |         |      |           |
| Dry mouth                            |         | 3       | 11    | 1       | 11    |         |      |           |
| Fever                                | 4      | 17      |       |         |       |         |      |           |
| Sexual problem                       | 1      | 19      | 1     | 11      |       |         |      |           |
| Weight gain                          |         |         |       |         |       |         | 1    | 11        |

### Table 5. Type of symptom management strategy and perceived effectiveness.

| Symptom                              | Time 1 (n = 735) | Time 2 (n = 519) | Time 3 (n = 557) | Time 4 (n = 499) |
|--------------------------------------|------------------|------------------|------------------|------------------|
| Medication                           | N (%) M effect   | N (%) M effect   | N (%) M effect   | N (%) M effect   |
| 403 (65.7)                           | 1.9 (0.9)        | 25 (30.9)        | 13 (2.9)         | 39 (28.9)        |
| Complementary/traditional treatments | 230 (37.0)       | 23 (28.4)        | 13 (2.9)         | 4 (3.0)          |
| Self-comforting                      | 250 (39.9)       | 23 (28.4)        | 13 (2.9)         | 4 (3.0)          |
| Change in diet                       | 377 (39.7)       | 17 (21.8)        | 4 (0.9)          | 1 (0.7)          |
| Seeking help                         | 241 (38.5)       | 17 (22.7)        | 8 (1.8)          | 2 (1.5)          |
| Exercise                             | 37 (5.9)         | 5 (7.4)          | 4 (0.9)          | 0                |
| Spiritual care                       | 208 (33.3)       | 45 (46.4)        | 20 (4.5)         | 2 (1.5)          |
| Daily thoughts/activities            | 233 (37.3)       | 21 (26.6)        | 5 (1.1)          | 0                |

Conclusions and implications

This study found a high symptom burden among HIV patients, which significantly decreased with progression on antiretroviral treatment. This means that antiretroviral treatment is effective in reducing the HIV-related symptom burden among HIV patients.
Several symptoms that persisted over time and several sociodemographic factors that were identified can guide symptom management using the existing WHO clinical guidance that emphasizes the essential role of palliative care alongside HIV treatment.

The utilisation of different symptom management strategies (medical, spiritual, complementary, and traditional) should be taken into consideration in HIV treatment.

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