RELIGIOUS BELIEFS AND DEPRESSION: PSYCHOSOCIAL FACTORS AFFECTING HIV TREATMENT OUTCOMES IN, SOUTH AFRICA

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ABSTRACT

Analysing factors associated with virological failure (VF) may improve antiretroviral therapy (ART) outcomes for individuals living with HIV. The Risk Factors for Virological Failure (RFVF) study compared 158 cases with VF (viral load, VL >1,000 copies/mL) and 300 controls with virological suppression (VL ≤1,000 copies/mL) after ≥5 months on their first ART regimen at McCord Hospital in Durban, South Africa between October 2010 and June 2012. RFVF participants completed a battery of various psychosocial measures. Using multivariate logistic regression stratified for gender, the association of various psychosocial factors with VF was assessed. It was found that not all factors were equally significant for both genders. The factors that were significantly associated with VF for both genders were younger age, shorter treatment duration and reporting depressive symptoms. The factors associated with



New Voices in Psychology Volume 12 | Issue 2 | 2016 | pp. 2–20 https://upjournals.co.za/index.php/NV https://doi.org/10.25159/1812-6371/2784 ISSN 1234-5678 (Print) © Unisa Press 2017 VF that differed by gender were religious inactivity, having HIV+ family members, and status disclosure to friends.

Keywords: antiretroviral treatment; gender; HIV/AIDS; psychosocial factors; South Africa; virological failure

INTRODUCTION

South Africa has more people living with HIV (over 6.4 million) than any country in the world as of 2012 (Shisana et al., 2014). The province of KwaZulu-Natal (KZN) continues to report the highest HIV prevalence (16.9%) of all the provinces of South Africa (Shisana et al., 2014). In 2004, the South African government commenced providing antiretroviral therapy (ART) free of charge for those who meet eligibility criteria, and currently South Africa has the largest public-sector ART programme in the world (Mutevedzi et al., 2010; Nachega et al., 2006).

A rapid increase of ART in sub-Saharan Africa has presented new challenges. such as identifying and managing virological failure (VF), in order to prevent the emergence of HIV drug resistance, clinical deterioration and death. An estimated 4.9% to 19% of patients on first-line ART experience VF in South Africa, using varying viral load thresholds (Barth et al., 2011; Barth et al., 2010; Boulle et al., 2010; El-Khatib et al., 2011; Gupta et al., 2008). The vast majority of these patients have drug resistance mutations to at least one class of antiretrovirals (Marconi et al., 2008). As more individuals initiate ART and remain on treatment for longer periods of time, VF will become a substantial challenge resulting in further HIV transmission of this potentially drug resistant virus. Furthermore, many countries are not able to monitor HIV-1 viral load (VL) and therefore often maintain patients on failing regimens for longer periods of time. This can increase the risk of drug resistance, clinical events and mortality. Although VF with drug resistance can be treated by switching patients to costlier and less tolerable second-line regimens, it would be advantageous to recognise the psychosocial and socioeconomic factors associated with VF and intervene early in order to prevent these downstream consequences.

In previous studies, various psychosocial factors have been described in connection with adverse health outcomes without a clear definition of the term, 'psychosocial'. Martikainen, Bartley and Lahelma (2002) suggest that psychosocial factors are influences that act 'between the fully social and the fully individual level', describing neither the structure of society nor the psychological characteristics of individuals but their intersection. Making a distinction between macro-, meso- and micro-levels of society, Martikainen et al., (2002) maintain that the term 'psychosocial' is essentially a meso-level concept amongst other social structures such as religion, family, and employment environment. These social structures are in turn modified by macro-social structures such as land ownership, legal and welfare structures, and income distribution. Similarly,

Kagee et al., (2011) describe Bronfenbrenner's (1972) Ecological Systems Theory which postulates that there are three environmental levels that affect human behaviour: the immediate level of the family with whom the individual relates; the level of social institutions such as health care, transport and local economy; and the third level of the larger cultural and political context in which people live. These authors clarify that health and health-related behaviours are associated with psychosocial factors located in or affected by social institutions at all levels. However, not all factors in each level should be considered 'psychosocial'.

Various studies have highlighted the role that psychosocial factors play in HIV treatment outcomes. The desire to obtain and maintain social capital, which includes trust, cooperation, reciprocity and sociability, may influence patient appointment and medication adherence in sub-Saharan Africa, thereby greatly increasing the risk of VF (Ware et al., 2009). Studies have also assessed how marital and other relationships, disruptions in these relationships, treatment supporters, HIV-related stigma and disclosure of HIV status might affect treatment adherence (Bhat et al., 2010; El-Khatib et al., 2011; Nachega et al., 2004; Nel & Kagee, 2011; O'Laughlin et al., 2012; Peltzer et al., 2010; Ware et al., 2009). Results from these studies vary, with HIV status disclosure being particularly complicated and dependent on culture and context (Crankshaw et al., 2014). With respect to mental health concerns, several studies have shown that depression and having depressive symptoms are highly correlated with poor adherence among ART users (Do et al., 2010; Etienne et al., 2010; Nakimuli-Mpungu et al. 2012; Nel & Kagee, 2011; Peltzer et al., 2010; Wagner et al., 2011). A recent metaanalysis indicated that the likelihood of achieving optimal adherence to ART was 42% lower among those with depressive symptoms compared to those without depressive symptoms (Uthman, et al., 2014). Substance abuse can likewise impact adherence by impairing memory, concentration and physical coordination, as well as through its associations with mental health issues that may affect adherence directly (Nel & Kagee, 2011). Finally, the relationship between religious beliefs and ART adherence in South Africa has not been clearly established. Some have found that religion can be a barrier to ART adherence, while others have found that religiosity is positively correlated with ART adherence (Hess & McKinney, 2007; Kagee & Delport, 2010; Kisenyi, Muliira, & Ayebare, 2013; Wanyama et al., 2007; Zou et al., 2009).

The Risk Factors for Virological Failure (RFVF) study in Durban, South Africa (Marconi et al., 2013) aimed to identify the most significant factors associated with VF among individuals receiving HIV treatment. Accordingly, a comprehensive survey including socioeconomic and psychosocial factors such as depression, stigma, religious, and adherence measures was conducted among 458 participants receiving ART in KZN, South Africa. Such a broad assessment was useful in order to inform clinical and programmatic management algorithms, but was not intended for a deeper, more nuanced understanding of certain risk factors and individuals at greatest risk. Therefore, this analysis, a sub-study of psychosocial data from the RFVF study, was performed

with the objective to explore possible mechanisms underlying the identified statistically significant psychosocial factors while recognising the limitations for proposing causality. In this analysis, each factor was examined separately by gender and for its relationship to other participant characteristics. Subgroup analyses by gender were proposed based on the results from the RFVF study showing differences in VF by gender and the higher prevalence of depression among women in South Africa (Tomlinson, Grimsrud, Stein, Williams, & Myer, 2009). Understanding these key factors can help direct future studies aimed at addressing psychosocial determinants within the context of gender with the goal of reducing the risk of VF.

MATERIALS AND METHODS

Study Design and Setting

The parent RFVF was a quantitative case-control study set at McCord Hospital (MCH) in Durban, South Africa. MCH is a regional referral centre that has been treating patients with ART since 2002. The President's Emergency Plan for AIDS Relief and South African government funding provided partial support for ART services which began in February 2004. A monthly fee (\$15 USD) was paid by patients for clinic services. Pill counts and pharmacy refills were recorded for each patient in the clinic. Routine viral load (VL) monitoring occurred at six month intervals and the ART regimen was maintained or changed depending on VL counts and levels of adherence.

Study Sampling

In brief, the purpose of the parent study was to identify predictors of VF for individuals with HIV receiving ART in this setting. Criteria for eligibility in the parent study were 18 years of age or older, HIV positive and receiving treatment at a McCord Hospital affiliated HIV clinic (study setting described in the supplement). Purposive sampling was used to select cases and controls. Cases were defined as patients on their first ART regimen for \geq 5 months who had a single VL measurement of > 1000 copies/mL. Controls (selected 2:1) were defined as patients on their first ART regimen for \geq 5 months with virological suppression (VL was \leq 1000 copies/mL). Eligible patients were identified through a file search. Permission to review files was granted by a waiver through McCord Research Ethics Committee and the Head of Medicine at MCH. All patients meeting the case definition were recruited as soon as the clinic staff identified patients meeting the appropriate criteria. Controls were subsequently recruited from within the HIV clinic during the same week. In total, there were 458 participants enrolled (300 controls and 158 cases). Enrolment and data collection commenced in October 2010 and ended in June 2012.

A research assistant, blinded to the case/control status of participants, administered a questionnaire in a semi-structured format in Zulu or English as preferred by the participant. The research assistant was formally trained for these instruments and interviewed the participants in a private research office. Major domains covered in the questionnaire included demographics, socioeconomic status, medical treatment and symptom history of participants. A battery of psychosocial assessments, including wealth, adherence, domestic violence, alcohol, food insecurity indices, neurocognitive testing (Singh et al., 2010), and the Kessler-10 questionnaire were administered during the interview with the participants (Marconi et al., 2013). The Kessler-10 measure is a 10-item self-report questionnaire intended to yield a global measure of "psychological distress" based on questions about the level of anxiety and depressive symptoms in the most recent 4-week period. In addition, research participants were asked information about their religious beliefs and affiliation. If they had a religious belief, they were asked to what extent they were engaging with their belief in their everyday lives. There were three open-ended questions asked of the participant upon the conclusion of the interview. These qualitative questions focused on adherence, clinic access and overall health.

Study data were collected and managed using REDCap electronic data capture tools hosted at Emory University (Harris et al., 2009). Emory University's Institutional Review Board and McCord Hospital Research Ethics Committee approved the study. Further details on the RFVF study can be found elsewhere (Marconi et al., 2013).

Statistical Analysis

Multivariate logistic models associated with VF were run for three different cohorts: the full sample, women only, and men only. All variables with a univariate p-value less than 0.10 overall or by gender were considered in each model. Age at ART initiation and duration of ART were forced into all models, and gender into the overall model, due to previously described associations with VF and adherence (Marconi et al., 2013; Wu et al., 2014). When similar variables had significant univariate p-values, these variables were compared and appropriately narrowed down for inclusion in the initial logistic models. Multicollinearity was assessed before evaluating each model. If multicollinearity was observed, variables with the highest variance decomposition proportions (those variables found to be collinear with other variables), were removed one at a time and the test was repeated until multicollinearity was no longer observed. We identified a final model utilising a backward selection procedure. Variables in the multivariate model with a p-value greater than 0.05 were removed one at a time until all remaining variables had a significant p-value. Likelihood ratio tests were performed when each variable was removed to assess whether the reduced model was significantly different from the full model

Next, significant variables (depression and religious beliefs) were selected from the multivariate logistic models to serve as outcomes of interest in order to identify the key population characteristics of those individuals possessing the important risk factors for VF. Univariate regression was then performed with the new "outcomes" as dependent variables and the remaining demographic and psychosocial factors as independent variables among the full sample and separately by gender. Variables with a univariate p-value of less than 0.10 were included in multivariate models assessing predictors of key psychosocial factors overall and among men and women individually. Final model selection was completed as described above, although age and treatment duration were not forced into each model. All data were analysed using SAS 9.3 (Cary, North Carolina, USA).

Results

Multivariate Analysis

Results from the multivariate analysis are shown in Table 1. In multivariate logistic models, the following variables were significantly associated with VF in the overall sample: male gender (OR=2.42, 95% CI 1.51-3.88), younger age (OR=0.83, 95% CI 0.72-0.94 for increasing 5 year age groups), shorter duration of treatment (OR=3.83, 95% CI 2.06-7.13 for those in the first quartile of treatment duration, ≤0.83 years, compared to those in that last quartile of treatment duration, ≥3.58 years), reporting any depressive symptoms (OR=2.21, 95% CI 1.35-3.61), being not active or having no religious belief compared to being somewhat or very active in their religious belief (OR=1.60, 95% CI 1.02-2.50), not always practising safe sex in the 6 months prior to enrolment (OR=2.50, 95% CI 1.17-5.32), having at least one HIV positive partner or family member (OR=1.70, 95% CI 1.03-2.82), having a treatment supporter (OR=2.02, 95% CI 1.13-3.64), and having one or more friends know their HIV status (OR=2.02, 95% CI 1.23-3.33).

Table 1: Psychosocial characteristics associated with HIV virological failure, McCord Hospital, Durban, SA, 2010-2012

| | Mode | 1: | | Mode | l 2: | | Model 3: | | | |
|-------------------------------------------------------------------------------------------------------|--------|-------------|------|------|---------|------|------------|-------|-------|--|
| | Full S | Full Sample | | | les Onl | у | Males Only | | | |
| Variables: | ORb | 95% C | CI | ORb | 95% (| CI | ORb | 95% (| CI | |
| Male Gender | 2.42 | 1.51 | 3.88 | - | - | - | - | - | - | |
| Age - adjusted 5 year age groups | 0.83 | 0.72 | 0.94 | 0.77 | 0.65 | 0.91 | 0.82 | 0.66 | 1.03 | |
| Duration of Treatment: | | | | | | | | | | |
| <=0.83 years | 3.83 | 2.06 | 7.13 | 4.13 | 1.82 | 9.40 | 5.38 | 1.84 | 15.72 | |
| 0.83 - 2.05 years | 1.33 | 0.71 | 2.50 | 2.00 | 0.90 | 4.47 | 0.99 | 0.33 | 2.96 | |
| 2.05 - 3.58 years | 0.91 | 0.47 | 1.76 | 1.44 | 0.62 | 3.33 | 0.63 | 0.21 | 1.88 | |
| 3.58+ years | Ref | | | ref | | | ref | | | |
| Reports any depressive symptoms in K-10 Questionnaire | 2.21 | 1.35 | 3.61 | 2.42 | 1.23 | 4.77 | 2.40 | 1.13 | 5.11 | |
| No religious belief or not active in their religious belief (vs. somewhat or very active) | 1.60 | 1.02 | 2.50 | 1.75 | 1.00 | 3.06 | | | | |
| In the last 6 months, practised safe sex often, sometimes, or never (vs. always) a | 2.50 | 1.17 | 5.32 | | | | | | | |
| Has a partner or family member(s) that are HIV positive (partner/spouse, child, other) | 1.70 | 1.03 | 2.82 | | | | 2.44 | 1.01 | 5.90 | |
| Has a treatment supporter | 2.02 | 1.13 | 3.64 | 2.49 | 1.19 | 5.20 | | | | |
| Had a family member who died of HIV | | | | | | | 2.98 | 1.29 | 6.91 | |
| Friend(s) knows they have HIV | 2.02 | 1.23 | 3.33 | | | | 3.67 | 1.46 | 9.23 | |

aExcluding one person with missing data on practising safe sex bOdds ratios were derived from logistic regression models

[&]quot;-" indicates not included in original model

[&]quot;..." indicates included in original model but did not survive selection process

In the gender-specific multivariate analysis, different factors were significant for men compared with women. Among women, younger age (OR=0.77, 95% CI 0.65-0.91 for increasing 5 year age groups), shorter duration of treatment (OR=4.13, 95% CI 1.82-9.40 for those in the first quartile vs. last quartile of treatment duration), reporting any depressive symptoms (OR=2.42, 95% CI 1.23-4.77), not being active or having no religious belief compared to being somewhat or very active in their religious belief (OR=1.75, 95% CI 1.00-3.06), and having a treatment supporter (OR=2.49, 95% CI 1.19-5.20) were all significantly associated with VF. Among men, shorter duration of treatment (OR=5.38, 95% CI 1.84-15.72 for those in the first quartile vs. last quartile of treatment duration), reporting any depressive symptoms (OR=2.40, 95% CI 1.13-5.11), having at least one HIV positive partner or family member (OR=2.44, 95% CI 1.01-5.90), having at least one family member who died of HIV (OR=2.98, 95% CI 1.29-6.91), and having one or more friends who know their HIV status (OR=3.67, 95% CI 1.46-9.23) were all significantly associated with VF.

Analysis of Key Psychosocial Factors

Of the statistically significant psychosocial factors identified in the overall multivariate analysis, having depressive symptoms and being active in religious beliefs were selected as outcomes for further multivariate analyses. These variables were selected because of their apparent significance in these and other models (Marconi et al., 2013) compared to other key psychosocial factors (having a treatment supporter, having family who died of HIV, practising safe sex in the last 6 months) as well as their potential for targeted interventions.

Depressive Symptoms

In multivariate analysis (Table 2), three factors were associated with depressive symptoms among the full sample: female gender (OR=1.71, 95% CI 1.12-2.59), having HIV-associated dementia (HAD) (OR=1.95, 95% CI 1.25-3.03), and having no income (OR=2.21, 95% CI 1.27-3.88). In multivariate analysis for women, the same factors remained significant as in the univariate analyses; having depressive symptoms was associated with the person most emotionally supportive living with the participant (1.90, 95% CI 1.08-3.35), disclosing HIV status to friends (2.44, 95% CI 1.20-4.95), having HAD (OR=2.19, 95% CI 1.20-4.01), and never drinking alcohol (5.01, 95% CI 1.13-22.15). In multivariate analysis among men, older age (OR=1.30, 95% CI 1.05-1.61 for increasing 5-year age groups), having no income (OR=6.25, 95% CI 1.71-22.80) and not being married or living with a partner (OR=2.00, 95% CI 1.00-4.03) were associated with having depressive symptoms. Among the responses to the openended questions, one case reported "my mind does not work properly all the time". This has been interpreted by the clinic psychologist to refer to feelings of depression. The controls on the other hand appeared to have overcome feelings related to depression.

One control reported "I was emotionally struggling but now things are better". Another control stated "I was emotionally not doing well because of things that happened to me in the past".

Table 2: Psychosocial characteristics associated with having depressive symptoms, McCord Hospital, Durban, SA, 2010-2012

| | Model 1: | | | Model 2: | | | Model 3: | | | |
|------------------------------------------------------------|----------|-------------|------|----------|---------|-------|----------|--------|-------|--|
| | Full S | Full Sample | | | Females | | | Males | | |
| Variables: | OR | 95% CI | | OR | 95% CI | | OR | 95% CI | | |
| Female Gender | 1.71 | 1.12 | 2.59 | - | - | - | - | - | - | |
| Age - adjusted 5 year age groups | - | - | - | - | - | - | 1.30 | 1.05 | 1.61 | |
| No income | 2.21 | 1.27 | 3.88 | - | - | - | 6.25 | 1.71 | 22.80 | |
| Person most emotionally supportive lives with you | - | - | - | 1.90 | 1.08 | 3.35 | - | - | - | |
| Any family members died of HIV | 1.57 | 1.02 | 2.42 | | | | | | | |
| Disclosed HIV status to friends | - | - | - | 2.44 | 1.20 | 4.95 | - | - | - | |
| Never drinks alcohol | - | - | - | 5.01 | 1.13 | 22.15 | - | - | - | |
| Not married or living with partner | - | - | - | - | - | - | 2.00 | 1.00 | 4.03 | |
| HIV Associated Dementia | 1.95 | 1.25 | 3.03 | 2.19 | 1.20 | 4.01 | | | | |

Having an Active Religious Belief

In multivariate analysis in the full sample (Table 3), having an active religious belief was associated with female gender (OR=2.45, 95% CI 1.58-3.80), older age (OR=1.15, 95% CI 1.02-1.30 in increasing 5 year age groups), being unemployed (OR=1.79, 95% CI 1.06-3.02), practising safe sex through abstinence (OR=6.34, 95% CI 1.37-29.41), having a current partner (OR=5.11, 95% CI 1.09-23.96), having biological children (OR=2.42, 95% CI 1.33-4.41), and never drinking alcohol (OR=2.44, 95% CI 1.29-4.65). Among females in multivariate analysis, never feeling nervous in the last month (OR=1.85, 95% CI 1.07-3.16), having biological children (OR=2.55, 95% CI 1.34-

4.84) and never drinking alcohol (OR=3.40, 95% CI 1.46-7.94) were associated with having an active religious belief. Among males, older age (OR=1.28, 95% CI 1.05-1.56 in increasing 5-year age groups), and never taking traditional medicine (OR=2.31, 95% CI 1.12-4.76) were associated with having an active religious belief.

Table 3: Psychosocial characteristics associated with being active in a religious belief, McCord Hospital, Durban, SA, 2010-2012

| | Model 1: | | | Model 2: | | | Model 3: | | | |
|-----------------------------------------------|----------|--------|-------|----------|--------|------|----------|--------|------|--|
| | Full S | ample | | Females | | | Males | | | |
| Variables: | OR | 95% CI | | OR | 95% CI | | OR | 95% CI | | |
| Female Gender | 2.45 | 1.58 | 3.80 | - | - | - | - | - | - | |
| Age - adjusted 5 year age groups | 1.15 | 1.02 | 1.30 | - | - | - | 1.28 | 1.05 | 1.56 | |
| Unemployed | 1.79 | 1.06 | 3.02 | - | - | - | - | - | - | |
| Never felt nervous in last month (K-10) | - | - | - | 1.85 | 1.07 | 3.16 | - | - | - | |
| Practises safe sex via abstinence | 6.34 | 1.37 | 29.41 | - | - | - | - | - | - | |
| Has any current partner | 5.11 | 1.09 | 23.96 | - | - | - | - | - | - | |
| Has biological children | 2.42 | 1.33 | 4.41 | 2.55 | 1.34 | 4.84 | - | - | - | |
| Never drinks alcohol | 2.44 | 1.29 | 4.65 | 3.40 | 1.46 | 7.94 | - | - | - | |
| Never taken traditional medicine | - | - | - | - | - | - | 2.31 | 1.12 | 4.76 | |

Discussion

This analysis identified several psychosocial factors associated with VF, some of which differed by gender, among ART patients at McCord Hospital. Within this sample of the clinic which was predominantly of Zulu origin and culture as well as Christian by self-report, the following were associated with VF among women: younger age, shorter treatment duration, reporting any depressive symptoms, not being active in religious

beliefs or having no religious beliefs (compared to being somewhat or very involved in activities related to religious beliefs), and having a treatment supporter. Many of the factors significant for women were not significant for men. Among men, additional risk factors found associated with VF included having more than one HIV-positive partner or family member, having more than one family member who died of HIV, and disclosing HIV status to friends. We then turned our attention towards the two most important risk factors (depression and religious beliefs) in order to determine how other factors were related to these two variables.

Depressive Symptoms

Depressive symptoms were associated with VF for both genders. Women with depressive symptoms were more likely to have disclosed their HIV status to friends, more often reported alcohol use and were more likely to have HAD. Men with depressive symptoms were more likely to be older, not married or living with a partner, and have no source of income. A systematic review of depression studies in sub-Saharan Africa found that achieving optimal adherence was 55% less likely among individuals on ART who had depressive symptoms (Nakimuli-Mpungu et al., 2012). In separate studies conducted in KZN, Botswana, and another in five African countries, adherence was lower among participants with higher depression scores (Do et al., 2010; Etienne et al., 2010; Peltzer et al., 2010). A study using longitudinal data from 14 sites involved in the Multi-site Adherence Collaboration on HIV (MACH14) found that adherence was negatively correlated with depression, and those with optimal adherence have significantly lower depressive symptoms than those with poor adherence (Wagner et al., 2011). Thus, the findings in this analysis are consistent with prior research.

While many study participants reported having depressive symptoms, few met the traditional thresholds for clinical depression on the Kessler-10 scale. Only 4.4% of the study population met the threshold for any depressive disorder, which is much lower than other prevalence estimates of 20-31% in sub-Saharan Africa (Etienne et al., 2010; Nakimuli-Mpungu et al., 2012). It is unclear whether this stems from a lack of clinical depression in this population, or whether the Kessler-10 scale is not a culturally and contextually appropriate tool to measure depression in this setting. The Kessler-10 measure has had mixed results in South Africa, with one study finding a large number of patients with good internal reliability and substantial participants with a disorder in a KZN township (Kuo & Operario, 2011). Another study found it "acceptable" for screening depression among pregnant women in Cape Town, identifying 66% of major depression cases (Spies et al., 2009). When Kessler-10 validity was assessed in a nationally representative household study in South Africa, Andersen, Grimsrud, Myer, Williams, Stein and Seedat (2011) found that it was less effective than in other settings, and had significantly worse discriminating ability among blacks than white, coloured, Indian or Asian groups combined. These differing scores may result from differing interpretation, differing expression of depressive symptoms among black South Africans

as opposed to the groups used for standardising the Kessler-10 assessment or potential confounding from neurocognitive impairment (Andersen et al., 2011).

Having a Religious Belief and Social Relationships

Not having a religious belief, not being active in one's religious belief, and having a treatment supporter were associated with VF among women, but not among men individually. Women with VF were less likely to report feeling nervous or alcohol use and more likely to have biological children. Both religious practice and treatment supporters involve a structured social network, whether it is organised religion or a predetermined treatment partner. Studies have shown that faith can play conflicting roles in ART adherence in sub-Saharan Africa. If religion serves as a network of social support, it may improve psychological wellbeing and thus play a positive role in ART adherence. For example, a study in Uganda found that religiosity and ART adherence were positively correlated (Kisenyi, Muliira & Ayebare, 2013). Another study found that an increase in spirituality/religiousness after being diagnosed with HIV is correlated with slower disease progression (Ironson, Stuetzle & Fletcher, 2006). However, other studies have found that religion can be a barrier to adherence and proper ART use. Zou et al. (2009) described how religious beliefs about HIV can contribute to fatalistic attitudes and passive resignation, which hinders participation in treatment. These authors likewise refer to a study in rural Mali where people who believed that AIDS was a punishment from God had more fatalistic attitudes (e.g. agreeing to the statement "I believe that if a person has HIV/AIDS most treatments will not change anything") than those who did not (Hess & McKinney, 2007). Another study in South Africa found that, in about 30% of the population aged 18 and over, a fatalistic attitude to protecting oneself against HIV/AIDS was characterised by lack of self-direction and lack of personal control or power over destiny or fate (Meyer-Weitz, 2005).

The belief that prayer can cure HIV may also challenge adherence to ART programmes. A study on ART adherence in Uganda found that six out of 558 (1.2%) patients discontinued their ART because they believed that their evangelical pastors' prayers had cured them of HIV (Wanyama et al., 2007). A qualitative study of patient advocates in South Africa found that some church leaders urged patients to use prayer to overcome illness rather than prescribed clinical treatments, and that sometimes patients would discontinue ART after receiving spiritual healing because they believed that they no longer needed medical treatment (Kagee & Delport, 2010). Since our study did not include patients who dropped out of care, we may have missed some patients who left the clinic for these reasons. Overall, religiosity and being active in a religious belief seemed to have a positive role in virological success within this setting, particularly among women.

Surprisingly, having a treatment supporter was associated with experiencing VF. This association could stem from patients having been identified as being at risk for poor

adherence and were therefore encouraged by a clinical provider, adherence counsellor or family member to find a treatment supporter. While the order of events is unknown in this study, the association between having a treatment supporter and VF is inconsistent with most reports in the literature. According to Nachega, Knowlton and Deluca (2006) treatment supporters are crucial to maintaining long-term support. They can provide support in a variety of ways, through financial and material support, instrumental or logistical support like transportation to the clinic and reminders and assistance in taking medication, and moral/emotional support (Nachega et al., 2006). Treatment supporters can help to destigmatise HIV/AIDS because they socialise with individuals living with HIV in public which can restore hope and reduce social difference in the person they support, and reduce social isolation among people living with HIV (O'Laughlin et al., 2012; Ware et al., 2009). Patients may want to maintain their adherence and health to sustain relationships with their treatment supporters, which then ensures that social relationships will exist moving forward to improve their long-term adherence (Ware et al., 2009).

Several variables related to social and family relationships were associated with VF among men but not women, specifically having a friend who knew the participant had HIV and having family members who are HIV positive or have died from HIV. Men may be more affected by family members being HIV-positive or dying of HIV because they might feel responsible for their infection, particularly with partners or children. When HIV inhibits a man's ability to maintain employment or care for their families, they may feel more guilt and low self-esteem from "failing" their families, leading to challenges with disclosure or treatment adherence (Fitzgerald, Collumbien & Hosegood, 2010). Additionally, men tend to be more concerned about the physical symptoms of HIV than women, so seeing family members suffer from HIV infection and death may arouse feelings of anxiety and depression affecting their daily functioning and immune response (author's psychological practice observations). It is also possible that having a family member, particularly a partner, die from HIV may indicate long-term infection and late initiation of ART with resultant poor treatment outcomes and VF.

Disclosure and Discrimination

Disclosing HIV status to friends, by choice or not, could lead to increased stigma, and thus compromise adherence and treatment outcomes. There is often a reluctance to disclose one's HIV status because of the fear of stigma, unsolicited disclosure of that status with others, the possibility of rejection, including economic abandonment and violence especially by a male partner of a woman (a woman is more likely to have been tested than a man within a relationship), and resultant social isolation (Kehler, Mthembu, Ngubane-Zungu, & Mtambo, 2012; Ncama, McInerney, Bhengu, Corless, Wantland, Nicholas, . . . Davis, 2008; Ware et al., 2009). Having experiences of discrimination were associated with lower adherence scores in a study in KZN (Peltzer et al., 2010).

In KZN, men feared disapproval and being ridiculed by other men if they disclosed their status (Fitzgerald, Collumbien & Hosegood, 2010). Studies in South Africa have found that patients who fear stigma and rejection from their family or friends as a result of disclosing their HIV status hide their medications, do not take their medication openly, and skip doses in order to avoid others observing them (Kagee & Delport, 2010; Nachega et al., 2004). Even if the patient had disclosed their status to family members, they may still not openly take medication because of feelings of shame and guilt within the family (Kagee & Delport, 2010).

Results indicate that factors affecting VF located at a micro- or individual level such as depression and disclosure interact with factors at meso- and macro- levels of society levels such as religious practices, employment opportunities and community discrimination. Hence, the use of 'psychosocial' in this study confirms Martikainen's suggestion that psychosocial factors are influences that act 'between the fully social and the fully individual level' (Martikainen, Bartley & Lahelma, 2002).

LIMITATIONS

Since the questionnaire was administered after patients had been diagnosed with HIV, the causal relationship of these associations cannot be established. Prior to enrolment, patients with VF may have experienced medical symptoms that could influence their psychosocial health and create issues that were not present prior to failing treatment. For example, symptoms of VF could cause participants to suffer depressive symptoms, rather than those depressive symptoms leading to changes in adherence that could lead to VF. One of the most statistically significant Kessler-10 questions asked whether participants felt tired during the last 4 weeks; this may be significant since fatigue is prevalent among people on ART and might be associated with a variety of other psychological and clinical factors (Jong, Oudhoff, Epskamp, Wagener, van Duijn, Fischer & van Gorp, 2010; Wagner et al., 2011). Due to the cross-sectional nature of the study, it is unclear when participants may have disclosed their HIV status to their partners, spouse, friends, or family, or when they might have established a treatment supporter. If a participant failing treatment is experiencing clinical symptoms, it may force them to disclose their status when otherwise they may not. In addition, participants knew their VF status at the time of enrolment, as it was necessary to identify cases eligible for the study. This may have influenced some of their symptoms and responses to the questionnaire but likely not substantially. Lastly, several of the estimates in this analysis are imprecise with wide confidence intervals. Future studies may require a larger sample size to confirm the associations and improve precision of psychosocial factors.

CONCLUSION

In conclusion, this analysis highlighted several key psychosocial factors that were experienced by patients with VF in this setting. Future studies should employ a longitudinal design to better understand the chronology and causality of depression, social support, disclosure, and religious belief with VF, and identify potential areas to improve treatment outcomes and psychosocial health among people living with HIV. As more people in South Africa and elsewhere remain on treatment for longer periods of time, it will become increasingly crucial to understand the nuances of risk factors that result in poor adherence and VF as well as identify ways to mitigate these outcomes.

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Conflict of Interest

No conflicts of interest were declared among the authors of this paper.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

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