An assessment of the prevalence and associated burden of symptoms in HIV patients in Swakopmund, Namibia

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Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
APCA	African Palliative Care Association
AZT	Zidovudine
BPI	Brief pain inventory
BQ	Barriers Questionnaire
CES-D	Centre for Epidemiological Studies depression tool
CFAR	Centre for AIDS Research
D4T	Stavudine
ECOG	Eastern Cooperative Oncology Group
EFV	Efavirenz
FTC	Emtrictabine
GDI	Global symptom distress index
HAART	Highly active anti-retroviral treatment
HADS	Hospital anxiety and depression scale
HIV	Human Immunodeficiency Virus
HRQOL	Health related quality of life
HSCL-25	Hopkins Symptom Checklist
ICESCR	International Covenant on Economic, Social and Cultural Rights
IQR	Interquartile range
LVP-r	Ritonavir boosted Lopinavir
MeSH	Medical subject headings
MOS-HIV	Medical Outcome Study-HIV

MSAS-SF	Memorial Symptom assessment scale-Short form
NGO	Nongovernmental organisations
NVP	Nevirapine
PEPFAR	President's Emergency Plan for AIDS Relief
PHYS	Physical symptom distress score
PLWHIV	Patients living with HIV
PMI	Pain management index
POS	Palliative outcome scale
PRISMA	Preferred reporting Items for Systematic Reviews and Meta-Analyses
PSYCH	Psychological symptom distress score
TDF	Tenofovir
3TC	Lamivudine
TMSAS	Total MSAS score
TOPCare	Treatment outcomes in palliative care
UNAID	United States Agency for International Development
VACS	Veterans Aging Cohort Study
WHO	World Health Organisation

Abstract

Background:

HIV infection and AIDS are characterized by a multitude of symptoms which has not changed since the advent of HAART. Based on this reality the World Health Organisation (WHO) recommends palliative care to be provided alongside disease specific treatment for all PLWHIV. There are many barriers to patients reporting their symptoms and physicians often fail to recognise the symptom burden.

Palliative medicine improves quality of life, relieves suffering, provides good end of life care and helps patients and loved ones to come to terms with a chronic progressive disease.

Namibia is one of the hardest hit countries globally with respect to the HIV epidemic. No palliative care services are available in that country yet. No research has been done to assess the prevalence and burden of symptoms amongst PLWHIV. The study serves as a pilot project to address these short comings.

Aim:

The aim of this study is to assess the prevalence and associated burden of symptoms in patients attending an HIV clinic in Swakopmund and local general practitioners' awareness of the symptom burden and assessment in HIV patients.

Methods

This was a cross-sectional descriptive study conducted at the HIV clinic at the State Hospital in Swakopmund, Namibia, and amongst general practitioners working in the Erongo region.

The study was conducted in two parts:

1) **Assessment of symptom prevalence and severity in HIV patients on HAART attending the HIV clinic at the Swakopmund State Hospital**
   A total of 104 adult patients were recruited using simple random sampling was used to recruit 104 adult patients who were interviewed using the MSAS-SF. Demographic data and symptoms recorded by the health care professionals during follow-up visits were extracted from the patients' records.

2) **The evaluation of general practitioners' perception regarding the symptom burden and importance of symptom assessment in HIV patients receiving HAART**
   Based on the outcome of the above findings a questionnaire was designed to assess the awareness of general practitioners of the burden of disease in PLWHIV.

Ethical Approval was obtained from the Human Research Ethics Committee of the University of Cape Town as well as from the Ethical Committee of the Ministry of Health, Namibia.

Results

The median of the sample was 40 years, the median CD4 count 417, and the median number of years on HAART was 4. The majority were females (61.5 %) and 66.3% were employed. The mean number of symptoms was 5.99 (median 5, SD 4.912). The most common symptoms were of psychological nature and pain, cough and peripheral neuropathy were common physical symptoms. Median values of TMSAS, GDI and PSYCH were higher in the unemployed and in females. PHYS was significantly higher in females. There was no association with the CD4 count. Time on treatment is not significantly related to any of TMSAS, GDI, PHYS or PSYCH scores, but younger age was related to higher GDI. Patient self-report of symptoms was significantly higher than symptoms recorded by the health practitioners during follow-up. Many general practitioners (44%) assume patients on HAART to be relatively symptom free, that low CD4 counts are related to symptom burden (84%) and that patients will report symptoms if present(76%).

Conclusion:

Symptom prevalence and burden is high in this study population despite HAART and there seem to be barriers to the reporting of symptoms by the patients. There is evidence of poor symptom assessment and symptom control. This highlights the need for palliative care for ambulatory HIV patients.

Introduction

In this chapter the reasons for high symptom prevalence in patients living with HIV (PLWHIV) are explored. Definitions for holistic care are provided and the need for palliative care in the management of HIV/AIDS is discussed.

Symptom prevalence and HIV/AIDS

HIV infection and AIDS are characterised by a multitude of symptoms. In the pre-ART era HIV/AIDS was a terminal condition and physicians could only provide palliative care, treating pain and other symptoms of advanced disease[1]. In first world countries HIV specific hospices and specialised services arose as a result of the AIDS epidemic[2] and in sub-Saharan Africa community based home care models were developed[3].

HIV has now become a chronic illness that can be managed by highly active anti-retroviral treatment (HAART)[4]. It is clear that antiretroviral treatment has greatly improved physical wellbeing in patients living with HIV, allowed a return to a high functioning life for many and improved survival; but it is still a progressive incurable disease[5].

Life expectancy and quality of life have improved; but mortality in patients with HIV remains higher than average and there is a rise in the number of deaths due to non-AIDS defining illnesses such as end stage liver due to Hepatitis co-infection, myocardial infarction and pulmonary diseases[6]. The initial decrease in mortality rates with the introduction of HAART has flattened[7] and mortality rates are on the rise again amongst socially disadvantaged patients[8].

HIV infection is symptomatic throughout the course of disease. The primary HIV infection usually presents as a flu-like illness that resolves again. This is followed by an “asymptomatic” period. In untreated HIV infections symptoms result from disease progression, decreased immunity and the resultant opportunistic infections. The latter can cause multiple symptoms such as mouth sores, neuropathic pain, breathing problems and gastroenteritis that can occur concurrently[9].

Pain and other chronic symptoms such as fatigue, anorexia, nausea and vomiting, dyspnoea and diarrhoea were common in the pre-HAART era[10] and still are today[11,12]. Prevalence is high regardless of CD4 counts, lack of opportunistic infections or the presence of HAART[13]. Only a third of these symptoms are detected by the treating physicians[13,10].

There is a high morbidity due to the disease itself and its co-morbidities. Many patients still present with advanced disease. The multi drug combinations are often toxic and associated with many side

effects[13]. There are more medical co-morbidities than come with normal ageing[9]. Cardiovascular disease, renal failure, liver cancer and brain impairment manifest more frequently as HIV treatment is started earlier[8]. HIV related malignancies have not declined with the use of HAART[14]. There is a higher incidence at a younger age at diagnosis of non-AIDS defining cancers[8].

Symptoms are subjective experiences and not only depend on physiological processes but also on the patients' interpretation thereof[9]. Most patients on HAART still remember the days when ART was not available and have seen or known people die of AIDS and this results in anxiety about their own health. New or persistent symptoms may be associated with treatment failure and fear of dying and increasing distress.

Anxiety about the treatment and the outcome, stigma, disturbed interpersonal relationships, fear of disclosure and secrecy are common psychosocial stressors, which amongst others result in a high prevalence of depression in patients living with HIV. That in turn can lead to worsening physical symptoms or somatisation and treatment non-adherence[9] and virological rebound[15].

The prevalence and burden of symptoms in PLWHIV is similar to that seen in other life threatening chronic illnesses. Based on that the World Health Organisation (WHO) recommended palliative care to be provided alongside disease specific treatment for all PLWHIV[12,16,16].

Definitions and declarations

The World Health Organization defines palliative care as "an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosomatic and spiritual"[17]. The WHO promotes palliative care as essential in HIV care from diagnosis to the end of life because of the high prevalence of symptoms throughout the disease trajectory[18]. A team, ideally comprised of nurses, social workers, doctors, spiritual counsellors and, in the African context of HIV/AIDS, community care givers, assists patients, their care givers and families[3].

Similarly, not specific to life threatening illnesses, holistic medicine is defined by the Canadian Holistic Medicine Association[19] as " a system of health care which fosters a cooperative relationship among all those involved, leading towards optimal attainment of the physical, mental, emotional, social and spiritual aspects of health".

These definitions embraces the concept of "total pain" defined by Cicely Saunders, the founder of the modern hospice movement, as the suffering that encompasses all of a person's physical, psychological, social, spiritual and practical struggles[20].

To integrate palliative care into existing health care systems the WHO used the framework of education, government policy and drug accessibility to develop a public health strategy[21,22]. A public health approach aims to improve health and quality of life of everyone in a community by introducing cost-effective and evidence-based interventions[22]. Palliative care is such an intervention which unfortunately is not available to a large proportion of the world's population[22]. At a congress in Cape Town for African palliative care trainers a consensus statement was drawn up, bearing in mind the many unmet needs of patients living with HIV/AIDS, cancer and other life threatening diseases in Africa. The Cape Town declaration[23] (Box 1) is based on the strategic pillars of the WHO.

1. Palliative Care is a right of every adult and child with a life-limiting disease.
2. Appropriate drugs, including strong opioids, should be made accessible to every patient requiring them in every sub-Saharan country and at all levels of care, from hospitals to community clinics and homes.
3. The establishment of education programs at all levels of the learning continuum; for all formal and informal caregivers, including medical and nursing trainees, community workers, volunteers and informal caregivers.
4. Palliative care should be provided at all levels of care: primary, secondary and tertiary. While primary care is emphasized, secondary and tertiary level teams are needed to lead and foster primary level care. This necessitates career opportunities for secondary- and tertiary-level palliative care professionals.

Box 1: Cape Town Declaration[23]

The World health assembly adopted the first-ever resolution on palliative care in 2014[24], calling for the integration of palliative care into national health services. The resolution clearly outlines recommendations to improve access and availability of hospice and palliative care, which include the integration of hospice and palliative care into national health services, budgets, and training in palliative care into the curricula for health professionals.

Palliative Care and HIV/AIDS

The "medicalisation of HIV/AIDS"[25] resulted in overlooking issues related to treating a progressive, incurable and ultimately fatal disease. The interest in new therapeutic options and in quantifying the response to treatment should not obscure that fact that there is a need for palliative care at all stages of HIV disease[4]. Symptoms are often unrecognised, either because health care providers do not ask or because symptoms are considered "subclinical"[13] - because they are not measurable or not obviously related to disease or disease progression. Unaddressed physical, psychological and

social symptoms, besides negatively influencing quality of life, have potentially severe clinical implications such as decreased treatment adherence, subsequent treatment failure, resistance and increased infectiousness as well as increased morbidity and mortality[26].

Based on areas of evidence in HIV/AIDS epidemiology, Harding et al[25] spelled out 5 key areas highlighting the continuing need for palliative care in PLWHIV: i) prevalence of symptoms, ii) higher mortality rates than in non-infected people, iii) additional co-morbidities associated with prolonged survival, iv) HIV related cancer risk and v) late presentation.

Patients require integrated pain and symptom control along-side HAART. Palliative medicine improves quality of life, relieves suffering, provides good end of life care- including addressing treatment failure and withdrawal of HAART if futile- and helps patients and loved ones to come to terms with a chronic progressive disease[25].

Namibian facts

Namibia is one of the hardest hit countries globally with respect to the HIV epidemic, the prevalence ranging from 4 to 33%, averaging 13.5%[27]. In 2003 with support of the Global Fund and the President's Emergency Plan for AIDS Relief (PEPFAR) the Namibian government implemented an antiretroviral program in Namibia's public health facilities[28]. After piloting free prevention of mother-to-child-transmission the antiretroviral program has now been rolled out to the entire country, with 90% of patients in need of antiretroviral treatment (ART) receiving it[28].

The AIDS epidemic was the impetus for nongovernmental organisations (NGO) to start home based care programs, which for a long time were the only services in Namibia approximating palliative care. A recent pilot study (to identify priorities and preferences of the Namibian public for end-of-life care) in form of street survey in Windhoek, the capital of Namibia, revealed amongst other things that a hospital and not a hospice or palliative care unit was the preferred place of death for the majority of participants[29]. This was more likely due to being unfamiliar with such units, which are not available in Namibia, than a true preference for hospital care.

The Namibian constitution does not have a clear right to health, but it states that "general rules of public international law and international agreements binding upon Namibia become part of the law of Namibia"[30]. One of these signed agreements is the International Covenant on Economic, Social and Cultural Rights (ICESCR). The ICESCR not only asserts that "the State Parties to the present Covenant recognize the right of everyone to the enjoyment of the highest attainable standard of physical and mental health", but also emphasises the need for "attention and care for chronically and terminally ill persons, sparing them avoidable pain and enabling them to die with dignity"[21].

In 2007 the African Palliative Care Association (APCA), sponsored by the United States Agency for International Development (UNAID)/Namibia, started to scale up palliative care in Namibia. It has now been integrated into the HIV and AIDS national health policy, but unfortunately has not been implemented yet. The 2014 National Guidelines for ART include a paragraph which only advises on regular monitoring for side effects of treatment and for progress of disease or presence of opportunistic infections; no advice is given as to the treatment of possible symptoms[31].

In public health services it is difficult to address all the determinants of poor health. Recently Namibian clinics have become nurse run. Treatment initiation, TB screening and basic symptom control are managed by trained registered nurses, who are, however, not allowed to prescribe scheduled drugs, including morphine. Only difficult cases are referred to the medical officers. It has been shown that personalised treatment with good doctor-patient concordance improves quality of lives and decreases symptom burden and distress[32]. Patients dependent on public health services do not have a choice of health care provider and might get treated strictly according to treatment guidelines, but have little opportunity to discuss treatment options.

With more than 11 indigenous languages being spoken in Namibia and with many foreign health professionals employed in the public service, language and cultural barriers to effective health care, amongst others, are immense. However, good symptom control should still be a priority. No studies could be found that assessed the symptom prevalence in patients living with HIV in Namibia.
It is assumed that the symptom burden of the Namibian people living with HIV is not less than elsewhere. The aim is to document their experience using the short form of the Memorial Symptom assessment scale (MSAS-SF) and comparing that to their health care providers' recognition thereof. By doing that it is hoped to create awareness amongst health care providers about the extent of the problem, and to encourage patients to report their symptoms, even if not specifically asked about them.

In the introduction the symptom prevalence amongst PLWHIV and the need for palliative care was discussed. The literature review below focuses on studies assessing symptom prevalence and burden amongst PLWHIV worldwide. The burden of ART is discussed as well as barriers to symptom control. Literature discussing the need for and the effectiveness of palliative care is also included.

Literature review

The aim of the literature review was to find published studies done and data collection tools used to document symptom prevalence and burden of patients living with HIV/AIDS. Reasons for poor symptom control were also sought. Special interest was shown towards studies done in southern Africa, particularly Namibia and South Africa, as these two countries have similar health systems and treatment guidelines for PLWHIV.

Electronic databases were chosen based on the likelihood of yielding useful information. Via EBSCO Host the following data bases were searched simultaneously during the period June 2013 to July 2015: Medline, Africa-Wide Information, CINAHL, SocINDEX, and PsycARTICLES all from 1990-2015. Google scholar and Pubmed, even though it mainly accesses Medline, were also searched.

MeSH (medical subject headings) terms used in various combinations and in union with HIV/AIDS/HAART were symptom/pain/prevalence/burden/assessment/recognition/under-treatment, pain. These terms in addition to "knowledge" and "barriers" in union with clinician/healthcare provider/physician with or without HIV/HAART were searched to find studies exploring reasons for under-treatment of symptoms in general and in PLWHIV specifically

With the advent of HAART quantitative aspects of HIV management and monitoring became more important than the human dimension of the disease as described by Selwyn and Arnold[1]. Despite decreased morbidity and mortality in patients who can access treatment, the symptom burden has not been eliminated.

Symptom prevalence in the Pre-/ Early HAART era

i) International studies

It is well known that patients living with HIV in the pre-HAART era were often symptomatic and had a high prevalence of pain syndromes as described amongst others by Vogl et al [33]. These studies are included as they give a good foundation for symptom assessment and management.

In the early days of ART availability, as part of an ongoing study of pain and quality of life of ambulatory AIDS patients in New York City, Breitbart et al assessed the presence and intensity of pain, associated factors and the impact on quality of life [10,34]. Despite being published in 1996 it is still quoted frequently in current literature [35,36,37]. The authors conducted an extensive literature review which highlights the scope of the problem of pain in AIDS patients, but all studies included in the review were either retrospective studies or used small patient samples. The Breitbart study was

a systematic prospective cross-sectional survey of a large diverse patient population (438 patients) and used validated data collection tools. It was one of the first studies to use the short form of the memorial symptom assessment scale (MSAS-SF), previously validated for cancer patients[38], to measure physical and psychological distress in AIDS patients. In addition, the brief pain inventory (BPI) -which consists of a number of questions regarding pain, its severity and its interference with daily life, as well as rating the pain relief obtained from treatment[39]- the Karnovsky Performance scale and the AIDS specific physical symptom check list were used. Only half of the patients were on some antiretroviral treatment, and 77% on treatment for opportunistic infections. Pain was reported by 62% of patients, of which 50% had severe pain. This was comparable to pain intensity typically experienced by cancer patients[10]. On the MSAS an average of 17.1 symptoms were reported and the average physical distress score rated as 1.2. Pain was excluded from the calculation of the latter to show that the physical distress score was directly related to the presence of pain. The presence of pain was associated with the number of concurring HIV related symptoms, lack of ART, disease progression and current treatment for HIV related diseases. The presence and intensity of pain significantly influenced the psychological distress and the quality of life [34].

In the same ongoing study the Pain Management Index (PMI), as derived from the BPI was used to assess whether analgesic therapy corresponded to the type and severity of pain according to the WHO guidelines[40]. This assessment was based solely on patient self-report and not validated by independent chart review or physician contact. Nevertheless, a negative PMI for over 80 % of patients gives a strong indication that pain is not adequately controlled. Interestingly, women, poorly educated people and patients infected by HIV due to intravenous drug use, were more likely to receive inadequate pain control. The authors[40] suggested the following barriers to providing adequate analgesia: poor knowledge of physicians regarding pain and management in HIV disease, stigma and discrimination associated with HIV disease and patient related barriers. The latter, including fear of addiction, side effects of treatment and beliefs about the illness, was shown to play a big role in under-treatment of pain in HIV infected patients[41].

ii) <u>Studies in Southern Africa</u>

Very little could be found about studies done in southern Africa on HIV/AIDS symptomatology in the pre-HAART era.

The study done by Norval [42] in 2004 seems to have been the first to investigate the symptom prevalence in HIV patients in South Africa. No literature review is evident, but similar studies done elsewhere were mentioned in the discussion. The study included 103 adult patients with WHO stage

4 AIDS, registered at the SOWETO hospice in Johannesburg. They were questioned on 26 symptoms and sites of pain. It is not clear how the list of symptoms were derived at. No sample size calculation was reported. But the study clearly showed that pain was highly prevalent (98%) and reported as the worst overall symptom in a third of patients. The commonest sites for pain were the lower limbs. Other common symptoms were weight loss, loss of appetite, low mood, weakness and dry skin. Despite its shortcomings the study highlighted the need for palliative care throughout the HIV disease trajectory.

Symptom prevalence and burden in the current treatment era

i) International studies:

In 2012 Merlin et al [43] achieved their aim of determining the prevalence and severity of symptoms and related risk factors in a population of ambulatory HIV patients. This study included 156 patients (the sample size was not elaborated on) that were selected from a large clinical cohort from the University of Pennsylvania's centre for AIDS Research (CFAR). Although not specifically mentioned, it was assumed that all participants were receiving HAART, as all of them had a viral load less than 1000 copies/ml. The BPI and MSAS-SF were used as data collection tools. Risk factors for the presence of pain were assessed by multivariate analysis. These factors assessed were: psychiatric illness, intravenous drug use, tobacco use, race, CD4 category and viral load. The types of HAART used weren't mentioned and not included in the analysis. Psychiatric illness and IV drug use were associated with higher MSAS subscale scores and patients with psychiatric illness were 40% more likely to have pain. The median number of symptoms was 8; common physical symptoms that also caused high distress were pain, lack of energy and tingling of hands and feet. More than half of the cohort experienced 4 out of the 6 psychological symptoms.

The researchers also did a chart review on the day of the interview to see whether pain was mentioned in the participants' progress notes and what treatment had been provided. Of the patients who reported pain during the study, this was documented in only 67% of cases, severe pain being more likely to be documented. Half of the patients receiving analgesics reported relief of pain.

Pain is a common symptom in PLWHIV[36] and many reports suggest that anxiety[44,15,26], depression[45-47] and fatigue[15] are common yet underreported[36].

A recently published review by Parker et al[48] focuses on the prevalence and characteristic of pain in PLWHIV, factors contributing to pain and pain management. Populations from low-income countries and females were found to be underrepresented in the studies. Prevalence rates of pain are between 50 and 67% throughout all stages of the disease and have not diminished over the 30 years

spanning the studies reviewed. It was noted that despite increasing awareness of the problem under-management persists .The comment by Harding et al[49], discussing some draw backs of the review, more clearly spells out associations with pain and symptom burden: "of sexual risk taking, poor adherence to ART, treatment switching, viral rebound, poor quality of life and suicidal ideation". Parker[50] responded by reiterating that the time has come to test and develop strategies to improve pain assessment and management rather than to identify and describe the problem of pain in PLWHIV.

ii) <u>Studies in Southern Africa</u>

Harding et al[51] were the first to report on the prevalence, burden and correlates of physical and psychological symptoms in HIV patients receiving palliative care in sub Saharan Africa. Researchers recruited 224 patients, 192 from South Africa and 32 from Uganda. The reason for the study sites in different countries and the choice of the sample size is not clear. The data collection tool was the MSAS-SF and additional physical symptoms, determined to cause distress in another study from Uganda, were added. It is of note that the mean number of symptoms was 18; the most prevalent symptoms were pain, feeling sad, feeling drowsy, worrying and lack of energy. Symptoms rated highest in severity were hunger, pain, loss of weight, numbness and lack of energy. All the MSAS subscales showed high levels of distress. Women and patients with poor physical functioning, as assessed by the Eastern Cooperative Oncology Group (ECOG) functional status score experienced higher symptom burden and distress. Being on ART did not change the symptom burden, emphasising the need for palliative care despite provision of ART.

It was hypothesised that prevalence of symptoms would be even higher in HIV patients not receiving palliative care; but in their discussion they mentioned a similar study done in Uganda by Wakeham[52] on HIV patients without access to palliative care in which symptom prevalence and burden were slightly less. These participants all had a CD4 count of less than 200 cells per micro litre and none were receiving ART. In the Harding study under discussion too few CD4 counts were available to make any useful comparisons.

Two papers were published in the SAMJ on a study done in 3 public sector HIV clinics in Johannesburg, South Africa. In the first paper Farrant et al[11] used the MSAS-SF to determine the prevalence and burden of symptoms in 365 patients (sample size calculation not included) of which 98% were on HAART. All 4 psychological symptoms (sad, irritable, worrying, feeling nervous) were amongst the ten most prevalent. Common physical symptoms were numbness and tingling in hands and feet, sexual problems, pain, "I don't look like myself" and lack of energy.

In the more detailed second paper describing the study conducted by Farrant et al[53] the 7 patients not receiving HAART were excluded from the study population. In addition to using the MSAS-SF, the physical performance for each participant was scored using the Karnofsky Performance scale (0=dead, 100=normal). A mean score of 90 indicated a high level of functioning but did not mean patients were symptom free.

This paper focussed on "Maintaining wellbeing for South Africans receiving ART: The burden of pain and symptoms is greater with longer ART exposure" and also explored additional associations of symptom burden with independent variables. Associations of the MSAS subscales were tested against the independent variables of age, gender, WHO stage, current CD4 count and count at start of treatment, current viral load, years on treatment and whether treatment was switched. Treatment combinations were not recorded. There was a consistent relationship between worse symptom indices and greater number of years on treatment. In addition WHO stage was associated with higher symptom burden and higher global symptom and psychological distress. Female gender and increased age were associated with higher physical distress scales.

In a very similar study done in Uganda, Namisango et al[54] investigated whether symptom burden is associated with treatment status, CD4 count and clinical disease stage. Patients with a low Karnovsky performance status had more symptoms and higher distress; psychological distress was high for patients with WHO stage 4 disease. ART and CD4 were not associated with symptom burden, but in contrast to the study above, men had higher symptom burdens. Symptom burden was not affected by level of education.

Psychological distress

i) International studies:

In a recent systematic review of literature Lowther et al[26] assessed the prevalence of depression, anxiety and experience of stigma in patients on HAART. The review was performed following the PRISMA (Preferred reporting Items for Systematic Reviews and Meta-Analyses) guidelines and the Loney quality appraisal tool was used to evaluate the paper quality. The more specific search items such as "depression", "anxiety" and "worry" were used but no less specific terms such as "psychological distress". Depression was defined as decreased mood, loss of interest or enjoyment and decreased energy; anxiety as excessive irrational fear or dread. A large number of different data collection tools (34) were used in the various studies, the most commonly used were the Beck Depression Index, Centre for Epidemiological Studies depression tool CES-D) and the Hospital anxiety and depression scale (HADS). However, some collection tools used, as for example the MSAS,

measure psychological distress, which does not necessarily amount to the diagnosis of depression or anxiety. A mean point prevalence of 33.6% was found for depression and 28.4% for anxiety, with higher values being found in low income countries. The figures, despite the heterogeneous sample characteristics, assessment tools and methodologies, were then compared to prevalence of depression/anxiety in 1) the general international population and 2) patients with other chronic conditions. It was concluded that depression and anxiety are highest amongst PLWHIV. Up to 80 % of patients experienced stigma. It was hypothesised that as stigma is associated with psychosocial distress, this could be a reason for the high depression/anxiety prevalence.

ii) Studies in Southern Africa

Kagee[55] reported on the prevalence of sub-clinical psychological distress amongst patients living with HIV, hypertension and/or diabetes. The study was not included in the above review. The participants were recruited from public health clinics in the Western Cape and were divided into 4 subsamples: patients living with hypertension (85), with diabetes (25), with both hypertension and diabetes (14), and with HIV (85). Sample size calculations were not included. The subsample of HIV patients was younger than the others, but almost all patients lived in relative poverty. The Hopkins Symptom Checklist (HSCL-25), a measure of emotional distress, was administered to all sub-samples. The scoring system was not explained, but the scores for all 4 groups were high and did not differ significantly from another.

Symptoms: Treatment or disease?

It is well known that poor adherence to HAART compromises its efficacy as described by Stone et al[56]. Adherence, in turn, is amongst others influenced by patient-reported symptoms and medication side effects as reported, amongst others by Ammassari[57], Cooper[58] and Berg et al[59].

Johnson et al[60] investigated not only the prevalence and burden of symptoms of 109 patients on HAART but also whether these were perceived as disease or treatment side effect related respectively. The validated HIV symptom index[61], similar to the MSAS tool, records the presence of 20 symptoms and “the amount of bother” on a Lickert scale 1-4. In this study the list was extended to 38 symptoms, apparently to capture a wider range of problems. The need for this, however, is not evident as some symptoms have been duplicated (e.g. upset stomach and diarrhoea). On the symptom checklists participants of the study indicated whether they attributed the symptom to the disease, the treatment, both or other causes. Subscales of the SF-36, a validated tool to assess quality of life and functioning, helped to determine quality of life with respect to general health, physical and social functioning respectively.

Upset stomach, nausea and vomiting, constipation, and alterations in taste sensation were most commonly attributed to side effects of treatment, whereas tender or enlarged lymph nodes/glands, night sweats, unintentional weight loss, fever, and loss of strength to the disease itself.

Impact of side effects, symptoms, and both were associated with impaired physical and social functioning. "In contrast to disease-related problems, symptoms attributed to side effects were not related to perceptions of general health. HIV-positive persons taking HAART make distinctions between symptoms of disease and side effects of treatment".

The participants were mostly male (80%) and had been on HAART for an average of 9 years. Although the results may not be generalizable, the study highlights the need to assess patients beliefs regarding the cause of their physical problems, as perceived disease and side effect-related symptoms have significant and unique associations with quality of life and with adherence to treatment[57].

In a similar study done in Germany, Kremer et al[62] examined gender differences in the causal attributions of symptoms. They found that men were more likely to attribute symptoms to the disease and were motivated to maintain a treatment regime, whereas women were risking non-adherence or switching treatment regime in order to avoid side effects.

As part of a study exploring the wider experience of living amongst gay men with HIV in the UK, Harding et al[35] assessed the symptom prevalence and burden as well as the association with the use of HAART in that very specific patient population. This was an online survey of 347 men, of which 57% were on HAART, recruited via gay websites, email lists and flyers at HIV clinics. It is not clear whether this really included all the HIV clinics in the UK. The MSAS-SF tool was used for the first time in a patient population with less advanced HIV disease and on HAART.

As in other studies symptom prevalence was high, especially for psychological symptoms, regardless of the use of HAART. Physical symptom prevalence was higher in HAART users. Of the 14 symptoms that were significantly more frequent amongst HAART users, most could be related to treatment side effects. HAART combinations of study participant were not specified. Of the independent variables age, years living with diagnosis, being on treatment (time on treatment was not considered), CD4 count and viral load, only the use of HAART was associated with higher number of symptoms and global (borderline significant) and physical distress indices. A lower CD4 count was weakly associated with higher global distress. Although not mentioned in the discussion of the study, the physical distress index was less than one for both groups of patients, which implies (see Methodology, MSAS-SF) that although present, the distress is not very significant.

The authors describe limitations of the study but these do not detract from the message that antiretroviral therapy is associated with symptom prevalence and burden.

In a similar study done in San Francisco, Lee et al[63] investigated how personal characteristics might influence symptom experience. The study sample was more ethnically diverse and predominantly male. They also found that ART users had a larger symptom burden than patients not yet receiving treatment. The MSAS distress scales, however, were lower than those measured in HIV/AIDS patients in the pre-HAART era[10,64]. The finding that the type of antiretroviral regime had no effect on the symptom burden was not validated. Nowhere in the paper were the ART combinations mentioned.

International[12] and local[31] HIV treatment guidelines now recommend the combination of Efavirenz (EFV), Emtrictabine (FTC) and Tenofovir (TDF) as first line regime in treatment-naïve HIV patients. Edelman et al[12] compared the symptom experience of patients on EFV/FTC/TDF with those on other treatment combinations and how that affected health related quality of life. The rationale of the research was to study an older HIV population with co-morbid disease, in this case veterans (1759 participants) that are part of the Veterans Aging Cohort Study (VACS). The study population, largely represented by black males, was also supposed to better reflect a routine clinical population than those participating in randomised controlled trials. The average age of these men was 54. Co-morbid disease was rated by the VACS index, which is a prognostic score for all-cause mortality and incorporates data on age, HIV and non-HIV biomarkers. However, co-morbid diseases expected in that age group such a cardiovascular disease and the respective treatment were not alluded to, and might have influenced the symptom experience. Even though the population was slightly older, the average time on HAART was only between 2-3 years. They did, however, show clearly that symptom burden, as assessed by the HIV symptom index, was less in patients on EFV/FTC/TDF and that they had an improved quality of life, as measured by the SF-12.

Underestimation, under-recognition, underreporting and under-treatment of symptoms

i) International studies

The "under-recognition and under-treatment of pain and other symptoms" is often stated and work done in the pre-HAART era by Breitbart et al[40] , as discussed before, and Fontaine, Larue and others[65,66] are still the most frequently quoted to substantiate the statement[39,53,37]:

In the first of the two reports by Larue, Fontaine and others[65] describing a large study done in France, prevalence and burden of pain was assessed using the BPI. Participants also had to rate their quality of life, but it is not clear what they were to base it on. Treating physicians were asked to

record the presence and rate the severity of pain, identify the source of pain and describe the treatment provided. Pain severity was underestimated in 52% of patients; underestimation being less likely in less severe pain and when a source for pain could be identified.

Based on the WHO guidelines a pain management index (PMI) was calculated to assess the appropriateness of analgesic treatment with respect to the severity of pain. The PMI was initially validated by Cleeland et al[67] amongst patients with metastatic cancer. When the PMI was based on patients' reports of pain severity 85% of patients were under-medicated, when based on the physicians severity assessment there were still 70% with negative prescription adequacy index scores.

The second paper by Fontaine et al[66] concentrated on the physicians' symptom recognition in HIV patients. A list of 16 physical and psychological symptoms common in HIV/AIDS was submitted to the patients, who rated each symptom according to its presence and severity. The same list was presented to the physicians and then symptom recognition rates and physician-patient agreement rates were calculated. Agreement rates ranged from 52% to 84%, with symptom recognition being better in ambulatory than inpatients and better in patients with poorer Karnofsky scales. Treatment side effects were not more likely to be recognised nor were symptoms amenable to treatment. In the discussion it was suggested that ambulatory patients might have been more verbal in voicing their complaints than the sicker inpatients. It was also suggested that the low recognition rates might have been exaggerated by poor recall bias. It is also possible that the symptom recognition was probably higher than the norm as physicians were more aware due to the study.

Edelman, Gordon and Justice published a similar study in 2011[16], but the work by Fontaine et al[66] was not included in the literature survey. The title "Patient and Provider-reported Symptoms in the Post-cART Era" is misleading as the term post-cART era is confusing and seems to imply up-to-date findings. It was, however, a secondary analysis of data collected from the Veterans Aging Cohort Study (VACS), an all male study, in 1999. The fact that 87% of participants were on HAART was only mentioned in the discussion and there was no mention about the type of treatment received.

Both patients and their health care providers were presented with the well validated HIV symptom index[61]. Patients rated the presence and burden of symptoms on a 5 point Lickert scale, while providers only indicated the presence/absence of these symptoms in the past 4 weeks. Health related quality of life (HRQOL) was assessed using the SF-12 and data regarding hospitalisation and mortality were collected from electronic medical records. Relationships between reported symptoms and quality of life, hospitalisation and survival respectively were assessed. They found, for

example, that patients that reported diarrhoea were less likely to die. No sample size calculations are available to prove that the percentage of participants that died (29%) was high enough to draw that conclusion. Patient reported symptoms that had a statistically significant correlation with outcome were compared to provider recognised symptoms. Using patient-report as gold standard, provider agreement was poor, with kappa scores less than 0.4 for all.

Despite certain shortcomings, the authors clearly showed that the reliability of provider recognised symptoms is poor and make a case for using tools to improve symptom recognition and management.

ii) Studies in Southern Africa

In a pilot study done in a district hospital in Durban, South Africa, Narasimooloo et al[39] investigated the prevalence, severity, recognition and adequacy of management of pain in a group of medical in-patients. This was adequately described in the abstract. Ethical approval was obtained from the relevant ethics committees. A convenience sample of 100 adult patients with a HIV related diagnosis was chosen for this descriptive study. The short form of the BPI was used to assess prevalence and severity of pain and its effect on the quality of life. By reviewing the patients' medical charts the documentation of pain and the treatment prescribed were assessed. The latter was compared to the severity of pain reported and the PMI calculated. A large proportion of patients (70%) had a CD4 count less than 200 and despite ART being available for free at government clinics, only 34% of the patients were on ART. The majority of patients (91%) reported the presence of pain, of which 70% was documented in the charts. A third of those patients reporting pain received no analgesics. In 66% of patients a negative PMI score was calculated, indicating inadequate analgesic treatment. This study again shows that pain recognition and management is poor. A strong case is made to use pain assessment tools in clinical practice and to explore barriers to adequate pain management.

Barriers to symptom control

i) International studies:

Clinicians' under-recognition and poor assessment often leads to under-treatment of symptoms and subsequent decrease in quality of life; but under-reporting and reticence to take medication also interferes with symptom control. Clinical assessment is more likely to focus on the disease and markers of disease management than on managing symptoms according to patient experience and symptom burden as reported by Resnik et al[68].

In order to determine factors preventing cancer patients from reporting pain and following treatment recommendations Ward et al[69] designed and validated a self-report Barriers Questionnaire (BQ), which has since also been used in other studies[70,41]. The following 8 concerns, based on previous literature, were thought to be barriers and the extent to which patients agreed with these concern was calculated: a) fear of addiction, b) concern about tolerance, c) concern about side-effects, d) fatalism, e) desire to be a "good" patient; i.e. not to annoy the physician, f) fear of distracting the physician from treating the disease, g) interpreting pain as disease progression, h) fear of injections.

Pain severity, adequacy of management, quality of life, as well as age, gender and level of education were compared to the BQ subscales. Patients who were under-medicated had significantly higher BQ scores. The most important finding was that many patients have misconceptions about using analgesics and that a large proportion of patients agreed that"good patients avoid talking about pain". In the discussion the importance about good communication and addressing concerns before patients complain of pain is spelled out. The same would be true for any symptom management.

Breitbart et al[41] were the first to assess patient-related barriers in the management of pain in AIDS patients. The authors modified the Barriers Questionnaire by adding the belief that pain medication might impair immune function (a concern that is also increasingly seen in cancer patients[70]) as well as the fear that analgesia impairs the ability to monitor illness symptoms. Fears of addiction and of side effects to opioids were the most frequently endorsed concerns. Higher BQ scores were found with higher total MSAS scores and were associated with under-treatment. They also came to the conclusion that patient-related barriers to symptom management add to the likelihood of under-treatment of AIDS related pain.

Breitbart et al[71] also assessed clinicians' perceptions of barriers to adequate pain management in patients living with HIV. Health care providers attending continuous education symposiums in 5 cities in the USA constituted a convenience sample for this study. The questionnaire packets they received consisted of i) demographic and clinical practice information, ii) questions that evaluated knowledge and attitudes with respect to pain management and iii) sixteen questions regarding perceived barriers to pain management. It is not clear how this list of barriers was derived at. Summary variables were created from the questions assessing **experience** in managing pain in AIDS patients, **knowledge** of the principles of pain management and **attitude** towards pain management. Higher scores in "attitudes" reflected more liberal attitudes toward pain management, including less avoidance of prescribing opioids. Associations of these variables were then tested against the barriers questions. Lack of knowledge of pain management, reluctance to prescribe opioids and

concerns about drug abuse were the most frequently endorsed concern, whereas patients' reluctance to report pain or to take opioids was less often seen as a barrier. Clinicians with more knowledge regarding pain management perceived patients' reluctance to report pain and excessive state regulations of prescribing analgesics as barriers, whereas the more experienced clinicians perceived very few of the suggested barriers as of concern. As these were only assessments of clinicians' perceptions of possible barriers there is no proven causal relationship to poor pain management.

The aim of a systematic review by Harding et al[72] was to identify inequalities in HIV palliative care and the associated barriers to access to such care. Although the introduction mentioned the host of symptoms and morbidities associated with HIV disease and HAART, the review mainly looks at terminal care. Search terms included terms representing all care models that include palliation. These were intersected with the union of (HIV/AIDS). Terms such as "barriers" or "unmet needs" were not included. The information gained was then assigned to barrier and inequity categories of patient, clinician, service and disease factors. Patient factors included barriers such as poverty, reluctance to address end-of-life issues and acceptance of suboptimal analgesia; lack of adherence to protocols, inadequate communication, fear of analgesia misuse/abuse and reluctance to address end-of-life issues were amongst barriers assigned to clinicians. Curative focus, lack of access to specialist pain management, stigma and discrimination were service factors in need of improving.

Land et al[73] looked at barriers to underreporting from another angle. They assessed what encourages or discourages PLWHIV from completing questionnaires by interviewing ten HIV patients attending a clinic in Birmingham. The importance of privacy was stressed; at the same time there were anxieties about missing the place in the queue at the clinic if one left to a separate location to complete the questionnaire. If patients were unsure about confidentiality and anonymity sensitive or personal information would not be disclosed. Questionnaires had to be quick and easy to complete and the aims stipulated clearly. Completing questionnaires only seemed worthwhile if assurance was given that and how it would improve future clinical practice.

ii) <u>Studies in Southern Africa</u>

In a more recent study done by Bogart et al[74] at a semi-private hospital in Durban barriers to care among people living with HIV in South Africa were investigated. Many patients are lost to follow-up after diagnosis and before ART is initiated. Qualitative data collected by semi-structured interviews from individual patients and focus groups were contrasted to those collected by similar interviews from healthcare providers. Stigma was a barrier to care endorsed by both groups. Patients had

concerns about ease of access to clinics, including long waiting times, as well as a non-caring attitude of the healthcare providers. The latter under-recognised patient dissatisfaction and it is fairly clear from that small study, that better communication (and resultant better understanding of concerns) is needed to facilitate patient satisfaction and retention in HIV care.

Palliative care and HIV/AIDS

i) International studies:

In a narrative review, which is an excellent work of reference for every health care provider dealing with PLWHIV, Selwyn[7] describes why and how palliative and disease-specific treatment for HIV should co-exist. Common symptoms and specifically pain syndromes and their aetiologies are discussed. Disease and symptom-specific interventions as well as possible drug interactions are dealt with. The potential risks and benefits of HAART in late stage HIV disease and the specific psychosocial issues for palliative care in the era of HAART are elaborated on. It is made clear that palliative care interventions are an important part of routine care of all HIV infected persons.

In a similar more recent review Fausto and Selwyn[44] more specifically discuss the needs of patients with advanced HIV disease in the current era of accessible HAART. The article reviews prognostic indicators of late-stage AIDS, trends in opportunistic infections, AIDS defining and non-AIDS defining malignancies and liver disease. It helps primary health care providers to identify patients that should be considered end-stage. The chronic disease status of the HIV infected as a result of HAART management and also the earlier onset of diabetes, lipid disorders, cancers and overall debility are discussed.

Harding et al[14] systematically reviewed the evidence base for the effectiveness of palliative care in PLWHIV from 1981 to 2003. Most data was generated in high income countries and in the pre-HAART era. It was clear that palliative care was effective in the management of pain, symptoms and anxiety and improved insight and spiritual well-being. Home palliative care and inpatient hospice care significantly improved patient outcomes. However, there was a lack of standardised experimental methods and a dearth of studies done in low-income/ sub-Saharan countries.

ii) Studies in sub-Saharan Africa:

To evaluate outcomes of integrated palliative care within HIV outpatient settings, Harding et al[75] compare patient outcomes at 2 clinics in Tanzania, which had similar patient populations and ART treatment and care programmes. Before the study was started, a multidisciplinary palliative care team was formed at one clinic (the intervention site). All HIV clinical staff at that clinic received a

minimum of one week with an ongoing training program in place. A supply of essential palliative care drugs, including morphine, was put in place, which was not the norm for the comparison site, where also no training took place.

At both clinics patients were recruited that had clinically significant pain or symptoms as assessed by the APCA African palliative outcome scale (POS) - the only symptom assessment tool validated in Africa[76]- which assesses prevalence of physical, psychological, emotional and spiritual problems in patients and their families and is adapted for a range of literacy skills. The medical Outcome Study-HIV (MOS-HIV) was used to measure quality of life. Sample size calculations were based on the APCA African POS pain score. Patients were followed fortnightly until week ten using the 2 self-report outcome tools. At the onset of the study the intervention site had better POS, physical health and mental health scores than the comparison site, as the palliative care clinical skills had been introduced before the study was started. All scores improved significantly more over time at the intervention site, and this improvement was not associated with CD4 count or ART. Even though the study is not randomised and the results may be overinflated, the study proves without doubt that simple palliative care training, support and drug availability in addition to standard HIV care improves the quality of HIV outpatients.

The protocol for a phase III randomised control trial with qualitative component was presented by Lowther et al[77]. The TOPCare (Treatment outcomes in palliative care) study was designed to assess the effectiveness of nurse-led palliative care interventions for patients on ART at 2 outpatient clinics, one in Mombasa, Kenya, and the other in Cape Town, South Africa. The intention is to provide scientifically sound evidence of this effectiveness and to aid in informing policy makers of the importance of including palliative care in general HIV care.

Summary of literature review

Many international studies as well those done in southern Africa highlighted high symptom prevalence, physical and psychological, and burden amongst PLWHIV in the pre- HAART as well as the current treatment era. Being on HAART did not change symptom burden and symptom indices worsened with increasing treatment time.

Pain is very common, under-reported, poorly recognised and inadequately treated. Poor pain and symptom control in general results in poor quality of life, poor treatment adherence and suicidal ideation. Impact of side effects, symptoms, and both were associated with impaired physical and social functioning.

A strong case is made to use pain/symptom assessment tools in clinical practice to improve symptom recognition and management as well as to explore barriers to adequate pain management. Patient related barriers to symptom control include concern about side effects, fear of addiction, interpreting symptoms as disease progression, accepting suboptimal care, fatalism and fear of distracting the physician from treating the disease. Barriers assigned to clinicians were lack of adherence to protocols, lack of knowledge of pain management, inadequate communication, fear of analgesia misuse/abuse and reluctance to address end-of-life issues. Curative focus, lack of access to specialist pain management, stigma and discrimination were service factors in need of improving.

It is made clear that palliative care interventions are an important part of routine care of all HIV infected persons. Palliative care was effective in the management of pain, symptoms and anxiety and improved insight and spiritual well-being. Minimal basic palliative care training of the clinic staff providing standard HIV care, continuing support of staff and palliative care drug availability improved the quality of life of patients attending HAART clinics in southern Africa significantly.

Rationale for the study

No studies could be found that assessed the symptom prevalence, burden or efficacy of management in PLWHIV in Namibia. This study serves to add to the knowledge of symptom prevalence and burden of HIV/AIDS in underdeveloped and under-researched countries. Of the available data collection tools the Memorial Symptom Assessment Scale (MSAS) was chosen as it has been used in many studies, including sub-Saharan Africa[11,51] to assess prevalence and burden of multiple symptoms in patients with cancer, AIDS or advanced medical illnesses[51]. The short form (MSAS-SF)[78,38] is easy to use, is not time-consuming and has useful subscale indices to calculate distress.

The outcome of an investigation into Health care providers' perceptions regarding symptom prevalence and assessment might assist in creating awareness of the suffering of PLWHIV as well as improved symptom assessment and management.

AIM

The aim of this study is to assess the prevalence and associated burden of symptoms in patients attending an HIV clinic in Swakopmund and local general practitioners' awareness of the symptom burden and assessment in HIV patients.

OBJECTIVES:

1) Assessment of symptom prevalence and severity in HIV patients attending a HAART clinic at the Swakopmund State Hospital
2) Investigation of symptom reporting by HIV patients on HAART during follow-up visits
3) Evaluation of local health care providers' perceptions regarding symptom prevalence and burden and the importance of symptom assessment in HIV patients receiving HAART.

METHODOLOGY

The study was conducted in 2 parts:

3) **Assessment of symptom prevalence and severity in HIV patients on HAART attending the HIV clinic at the Swakopmund State Hospital**
4) **The evaluation of general practitioners' perception regarding the symptom burden and importance of symptom assessment in HIV patients receiving HAART**

Study design and study site

This was a cross-sectional descriptive study conducted at the HIV clinic at the State Hospital in Swakopmund, Namibia, and amongst general practitioners working in the Erongo region.

Study population

1) **HIV patients:**

   The study population consisted of HIV patients on HAART attending the dedicated HIV clinic of the Swakopmund State hospital. The latter provides HAART to 3000 patients living in and around Swakopmund and which are not privately insured.

2) **General practitioners:**

   Swakopmund is part of the Erongo region of Namibia. Non-specialist doctors providing HIV care working in the public and the private health sector formed the study population for the second part of the study.

Inclusion and exclusion criteria

1) **HIV patients**:

   Patients 18 years and older on HAART attending the HIV clinic on study days and consenting to study participation were included in the study.

2) **General practitioners:**

   All medical officers working at the State Hospitals and private practitioners practising in the Erongo region were invited to take part in the study. Specialists were excluded from the study because no specialists are employed in the public sector of the Erongo region and none of the private specialists in the region are actively involved in providing HAART.

Sample size

1) HIV patients

A minimum sample size of 96 was calculated before data collection according to the following formula:

$$n = \frac{p(1-p)z^2}{d^2}$$

where n= sample size

p=anticipated patient proportion

d= precision on either side of the proportion

z=1.96, when calculating with a confidence interval of 95%.

Previous studies using the MSAS-SF have shown a median symptom prevalence ranging from 4 to 10 of 32 queried. The pain prevalence of about 50% in several studies was used for the anticipated population proportion (p= 0.5) being symptomatic, allowing for a range from 40% to 60% (d= 0.1).

2) General practitioners

All 35 general practitioners and medical officers working in the Erongo region had available email addresses and were invited to take part in the study.

Sampling

HIV patients

Simple random sampling took place on study days by inviting every fifth patient that came to the clinic for follow-up treatment to participate. If a patient declined, the patient next in line was invited.

Data collection

- Data collection tools:

1) HIV patients:

i) The Memorial Symptom Assessment Scale- Short Form (MSAS-SF) (Appendix 1)

The MSAS-SF was used to measure the prevalence and associated burden of symptoms over a 7 day period. It is a validated patient-rated data collection tool, the short form of which rates the severity, frequency and distress associated with 32 prevalent physical and psychological symptoms over a 7 day period [78,38]. The distress caused by the physical and psychological symptoms are rated on a 5-point (0-4) Likert scale. Zero is assigned to symptoms that are not present.

Separate subscales can be calculated [38,33]:

1. Global symptom distress index (GDI): an average of the symptom scores for 4 psychological symptoms (feeling sad, worrying, feeling irritable, feeling nervous) and 6 physical symptoms (pain, lack of energy, lack of appetite, feeling drowsy, constipation, dry mouth)
2. Physical symptom distress score (PHYS): an average of 12 prevalent physical symptom scores (pain, lack of energy, lack of appetite, feeling drowsy, constipation, dry mouth, nausea, vomiting, change in taste, weight loss, feeling bloated, dizziness)
3. Psychological symptom distress score (PSYCH): an average of 6 prevalent psychological symptoms scores (feeling sad, worrying, feeling irritable, feeling nervous, difficulty sleeping, difficulty concentrating)
4. Total MSAS score (TMSAS): an average of the symptom scores of all 32 symptoms

The potential range of these scales is from zero (minimal distress) to four (maximal distress)[33], and a score greater than one implies the presence of significant distress[38].

The subscales PHYS, GDI and TMSAS have been correlated with extend of a disease, but GDI, PHYS, PSYCH and the total number of symptoms can also be correlated to quality of life[51,79].

ii) Data extraction tool (Appendix 2)

A data collection form (Appendix 2), which was based on data collection tools used in similar studies[43,53], was drawn up to collect the following data from the patients' clinic cards (a patient record that accompanies the patients):

Demographic data: age, sex, employment status, CD4 count, viral load, years on treatment, HAART regime; these were chosen to determine whether there is a relationship between the data and the symptoms reported in the MSAS.

Symptom reporting: any symptoms that the study participant complained of during the previous 4 months of clinic visits as well as on the study day were recorded, together with the treatment received.

Pilot study of data collection tools:

The clinic staff members (nursing sisters and voluntary HIV counsellors) were used to pilot the data collection procedure and the questionnaire for clarity and coherence. A registered nursing sister working at the HIV clinic was initially assigned to help with administering the MSAS-SF and filling in the demographic data. During a small pilot study with 10 patients (not included in the results) it became clear, that the familiarity of the patients with the clinic sister deterred them from answering the questions truthfully. A retired nursing sister was then employed to help with the study.

2) General practitioners

iii) General practitioner Questionnaire (Appendix 3):

The original aim was to assess general practitioners' symptom recognition and appropriateness of treatment based on the outcome of the symptom assessment of the study population above. It turned out, however, that hardly any symptoms were reported in the clinic cards despite quite a few being reported in the MSAS questionnaire. Instead, after discussion with the supervisor, a questionnaire was designed as a preliminary investigation to assess the awareness of general practitioners of the burden of disease in patients living with HIV and their opinions on the need for proper assessment and treatment of symptoms in conjunction with treatment of HIV with HAART treatment. The design was an attempt to find some answers to why symptom assessment was virtually non-existent and what influence general practitioners' views could have on the big discrepancy between true symptom report and MSAS questionnaire reporting. Two retired general practitioners were used for a pilot study to test the questionnaire for comprehensibility.

- Data collection procedure:

1) HIV patients

The clinic staff members (nursing sisters and voluntary HIV counsellors) were briefed about the study and regarding confidentiality. A retired nursing sister was employed to help with the study. She was trained in research ethics and the study protocol.

The information sheet (appendix 4), the questionnaire (appendix 1) and the consent form (appendix 5) were translated into Afrikaans, Oshivambo, Oshiherero, and Khoekhoegowab by forward and backward translation and were administered in the language of choice of the study participant.

Information sheets were left in the clinic waiting room for patients to browse through at their own leisure. Eligible patients were approached by the HIV counsellors to take part in the study when they reported for their follow-up visits. Interviews were held in a separate room at the HIV clinic. The study was then explained by the research nurse in line with the information sheet (appendix 4). She then checked the understanding of the patient and gave an opportunity to ask questions. The fact that participation in the study and consent were voluntary was reiterated. Assurance was given that they could withdraw at any stage without influencing their care and that all data would be treated strictly confidential before consent was signed by the patient.

The short form of the Memorial Symptom Assessment Scale (MSAS-SF) (appendix 1) was then administered. Because literacy could not be assumed in the study population, the research nurse read out the questions while participants could also read the questionnaire and entered the responses. Only in Oshivambo speaking patients who could not read or speak one of the other languages, an HIV counsellor read out the questions and translated the responses. Even though the study participants were given the choice of their own language most patients wanted to communicate in English or Afrikaans.

Patients in Namibia making use of the public health system all carry their clinic cards with them. These are supposed to contain all the records of clinic visits, including patients' complaints, blood results and medications prescribed. In addition HIV clinics keep separate folders containing data specific to the HIV management of the patients. The consent form included a request to have access to that information during the interview. Data extracted by the research nurse were the demographic data, most recent CD4 count and viral load, records of symptoms reported by the patient during the clinic visits on the study day and in the preceding 6 months, as well as measures taken by the health care professionals to address the symptoms (appendix 2).

2) **General Practitioners**

The questionnaire and an accompanying letter (appendix 3) that explained the essence of the study was sent by email to all general practitioners treating HIV patients in private and public health services in the Erongo region, Namibia, with the request to fill out the questionnaire and to return it to the sender. A list of names and addresses were obtained from the local independent practitioners association and the Erongo regional office respectively. Two follow-up reminder mails were sent to improve the response rates.

- Data storage and Confidentiality

1) **HIV patients**

The consent forms containing the patients' names and study numbers and the questionnaires containing the study number only were stored separately. The questionnaires are stored separately from the consent forms in a locked filing cabinet in the researcher's office for future reference. The study computer is password protected.

2) **General Practitioners**

The completed questionnaires were printed out and numbered. After extracting the data they were stored in the same filing cabinet as the questionnaires above.

- Data analysis:

1) **HIV Patients:**

The data was entered into a purpose designed Excel spreadsheet, and subsequently imported into SSPSS for analysis. Descriptive data were generated for the patient characteristics and MSAS-SF scores. Prevalence and associated burden for each item and the subscale scores of global, physical and psychological scores were calculated.

The latter 4 scores were used as dependent variables in a univariate analysis to test the association with the following independent variables: age (continuous), employment (two levels of yes/no), CD4 count (2 levels of <=350/>350), gender (two levels of female/male) and months on treatment (continuous).

2) **General Practitioners:**

Data were entered into an Excel spreadsheet and then analysed using IBM SPSS Statistics for windows.

Ethical considerations

Ethical approval

Ethical approval for the research was requested and obtained from the Human Research Ethics Committee of the University of Cape Town (appendix 6) as well as from the Ethical Committee of the Ministry of Health, Namibia (appendix 7) before requesting and receiving permission from the Erongo regional office and the principal medical officer of the Swakopmund hospital to use their facility for the research (appendix 8).

Protection of vulnerable population

"Vulnerable persons are those who are relatively (or absolutely) incapable of protecting their own interests. More formally, they may have insufficient power, intelligence, education, resources, strength or other attributes to protect their own interests"[80]

HIV patients attending state clinics are a particularly vulnerable group of people. Not only does the stigma attached to HIV make patients fear lack of confidentiality; poverty, language barriers, lack of education, limited health facilities and lack of knowledge regarding scientific western medicine make this group of people extremely vulnerable to exploitation [81].

The information sheet (appendix 5) given to the patients to read and to take home contains most measures taken to protect the study population as well as the ethical considerations regarding the study:

- Information given to the participants before they sign consent should be given in a culturally appropriate way and in the local language [82]. The information sheet, questionnaire and consent form were translated into Afrikaans, Oshivambo, Oshiherero and Khoekhoegowab and the content of the information sheet discussed in the study participant's language.
- Voluntary participation in the study as well as the right to withdraw trial without reprisal and without having to give a reason was reiterated

- The community should receive fair benefits from the study, be it financial or in the form of education, improved health services or employment[81]. Even though there will be no direct benefits for the participants, the results of the study will be displayed in the form of a poster at the clinic. It might encourage better doctor-patient communication with resultant better symptom control.
- Contact numbers were provided to the study participants in case of problems or questions

RESULTS

Part 1: HIV patients

Sample characteristics

During the four week data collection period 110 participants were enrolled in the study. Three female patients withdrew consent after completing the questionnaire because they wanted to discuss participation with their partners first. Although arrangements were made for a renewed discussion, they did not return. One participant, known with bipolar mood disorder, was excluded because she was psychotic at the time. She was referred to the clinic medical officer for management. In two cases the symptom data were incomplete.

The clinical and demographic characteristics of the 104 participants included in the final sample are presented in Figure 1.

The mean age of the sample was 39 years (SD=9 years; minimum=19, maximum =60). The majority (61.5%) of the participants were females. The overall employment status was 66.2%; 80% of the males and 57.8% of the females were employed.

Figure 1: Demographic and Clinical Characteristics of the Sample

	Minimum	*Percentile 25*	*Median*	*Percentile 75*	*Maximum*	*Mean*	*Standard Deviation*
Age	19	33	40	45	60	39	9
CD4	82	281	417	544	1566	444	230
Months on Rx	1	16	40	75	162	48	35

		Count	*% N=104*
	Female	64	61.5
	Male	40	38.5
Employed	No	35	33.7
	Yes	69	66.3
CD4	<350	40	38.5
	>=350	64	61.5

*gender * Employed Crosstabulation*					
			Employed		Total
			No	Yes	
Gender	Female	Count	27	37	64
		% within gender	42.2%	57.8%	100.0%
		% within Employed	77.1%	53.6%	61.5%
	Male	Count	8	32	40
		% within gender	20.0%	80.0%	100.0%
		% within Employed	22.9%	46.4%	38.5%

The average time on HAART was 3-4 years (median 40 months; mean 48 months; minimum 1, maximum 162).

Eight different treatment regimes were found amongst the participants (Table1). Despite the availability of the fixed dose combination regime Tenofovir (TDF)/Emtrictabine (FTC)/Efavirenz (EFV), not even participants recently started on ART received it. The most commonly prescribed combination was Tenofovir (TDF), Lamivudine (3TC) and Nevirapine (NVP); 3 patients even still received Stavudine (D4T).

Table 1: HAART regimes

Treatment regime	Valid N
AZT/3TC/EFV	8
AZT/3TC/NVP	23
D4T/3TC/EFV	1
D4T/3TC/NVP	2
TDF/3TC/AZT/LVP-r	3
TDF/3TC/EFV	24
TDF/3TC/NVP	42
TDF/D4T/NVP	1
Total	104

AZT=Zidovudine;; 3TC=Lamivudine; D4T=Stavudine; TDF=Tenofovir; LVP-r=Ritonavir boosted Lopinavir; NVP=Nevirapine; EFV=Efavirenz

The latest mean CD4 count was 444 (median 417; SD 230, minimum= 82, maximum =1566). 38.5% had a CD4 count of less than 350, which was the cut-off value at the time for starting HAART. Although regular viral load testing had been introduced at the clinics shortly before data collection, not enough participants had recent values available for inclusion in the study. Only 32 viral loads were available. Although all of those study participants had been on treatment for more than a year, only four had a viral load less than or equal to 20. Of the five patients that had a viral load above 1000, only one was receiving second line treatment.

Symptom Prevalence and Distress

The mean number of symptoms was 5.99 (median 5, SD 4.912, minimum=0, maximum=20) (Table 2). A third of participants had 8 symptoms or more. Only ten patients (9.6%) were symptom free.

Table 2: Symptom prevalence and statistics

Nr of symptoms	Frequency	Percent	Cumulative percent
0	10	9.6	9.6
1	11	10.6	20.2
2	9	8.7	28.8
3	8	7.7	36.5
4	9	8.7	45.2
5	12	11.5	56.7
6	7	6.7	63.5
7	6	5.8	69.2
8	6	5.8	75.0
9	3	2.9	77.9
10	3	2.9	80.8
11	3	2.9	83.7
13	6	5.8	89.4
14	4	3.8	93.3
15	3	2.9	96.2
16	1	1.0	97.1
17	1	1.0	98.1
20	2	1.9	100.0
Total	104	100.0	

Symptom prevalence statistics

Total Symptoms	Mean	5.99
	Median	5.00
	Variance	24.126
	Std. Deviation	4.912
	Minimum	0
	Maximum	20
	Range	20

The most common physical symptoms were pain, cough, difficulty concentrating, difficulty sleeping, lack of energy, numbness /tingling in hands and feet, feeling bloated, dry mouth, problems with sexual interest and itching. There were 44 (42.3%) participants who reported pain which caused almost half of those to suffer from high levels of distress. Sweating, although not amongst the most frequently occurring symptoms, scored high on the distress scale (Table 3, 4).

Psychological symptoms were reported more frequently than physical ones and caused high levels of distress when present (Table 3, 4). All symptoms used to calculate the psychological distress score (PSYCH) are amongst the 10 most commonly occurring symptoms overall: **worrying**, **feeling sad**, pain, **feeling irritable**, **feeling nervous**, cough, **difficulty concentrating** , **difficulty sleeping**, lack of

energy and numbness/tingling in hands and feet. Feeling nervous was the only one of the psychological symptoms that did not fall amongst the highest scoring high distress symptoms

Table 3: Symptom frequency

Physical symptom	Occurrence total (N)	percent	High distress (N)*	Percent with high distress**	MSAS score/ high distress***
Pain	44	42.3	21	47.7	79.2
Cough	30	28.8	7	23.3	28
Difficulty Concentrating	27	26.0	8	29.6	30.4
Difficulty Sleeping	25	24.0	11	44.0	41.6
Lack of Energy	25	24.0	8	32.0	30.4
Numbness/ Tingling	25	24.0	5	20.2	20
Feeling Bloated	23	22.1	6	26.0	20.8
Dry Mouth	22	21.1	5	22.7	18.4
Problems with Sexual Interest	20	19.2	4	20.0	16
Itching	20	19.2	7	35.0	26.4
Sweats	19	18.3	8	42.1	31.2
Psychological symptom					
Worrying	51	49.0	21	41.2	71
feeling sad	45	43.3	15	33.3	50
Feeling irritable	43	41.3	9	20.9	30
Feeling nervous	33	31.7	7	21.2	23

***quite a bit and very much/ frequently and almost constantly**
****percentage of those reporting the symptom**
*****sum of high distress scores 3.2+4 or 3+4**

.

Table 4: Most common symptoms

	According to occurrence	According to high distress	According to MSAS score
1	worrying	pain	Pain`
2	Feeling sad	worrying	worrying
3	Pain	Feeling sad	Feeling sad
4	Feeling irritable	Difficulty sleeping	Difficulty sleeping
5	Feeling nervous	Feeling irritable	Sweats
6	Cough	Difficulty concentrating	Difficulty concentrating
7	Difficulty concentrating	Lack of energy	Lack of energy
8	Difficulty sleeping	sweats	Feeling irritable
9	Lack of energy	Cough	Cough
10	Numbness/ tingling	itching	Itching

The MSAS scores give an indication of the level of symptom distress and of quality of life. Even though the average scores are all less than 1 (Figure 2), indicating minimal distress, there were participants with very high distress scores, psychological distress being the highest. A quarter of the participants had a global distress index equal to or above 1; high psychological distress was found amongst 40 of the participants.

Figure 2: MSAS scores

	Valid N	Minimum	Maximum	Mean	Standard Deviation	Median	Percentile 25	Percentile 75
TMSAS	104	.00	1.88	.42	.40	.32	.15	.59
GDI	104	.00	2.94	.67	.66	.56	.13	.97
PHYS	104	.00	1.93	.39	.45	.27	.00	.57
PSYCH	104	.00	3.43	.80	.87	.47	.00	1.33

Frequencies of significant distress (>=1 is significant)

Variable	>=1	<1	total
TMSAS	10	94	104
GDI	25	79	104
PHYS	11	93	104
PSYCH	40	64	104

Associations with symptom burden indices

For the variables employment status (yes/no), sex (female/male) and CD4 count (<350/>=350) the Mann-Whitney U test was used to test their associations with the MSAS-SF scores (Table 5). The continuous variables age and months on treatment were tested using the Spearman's rho test (Table 6).

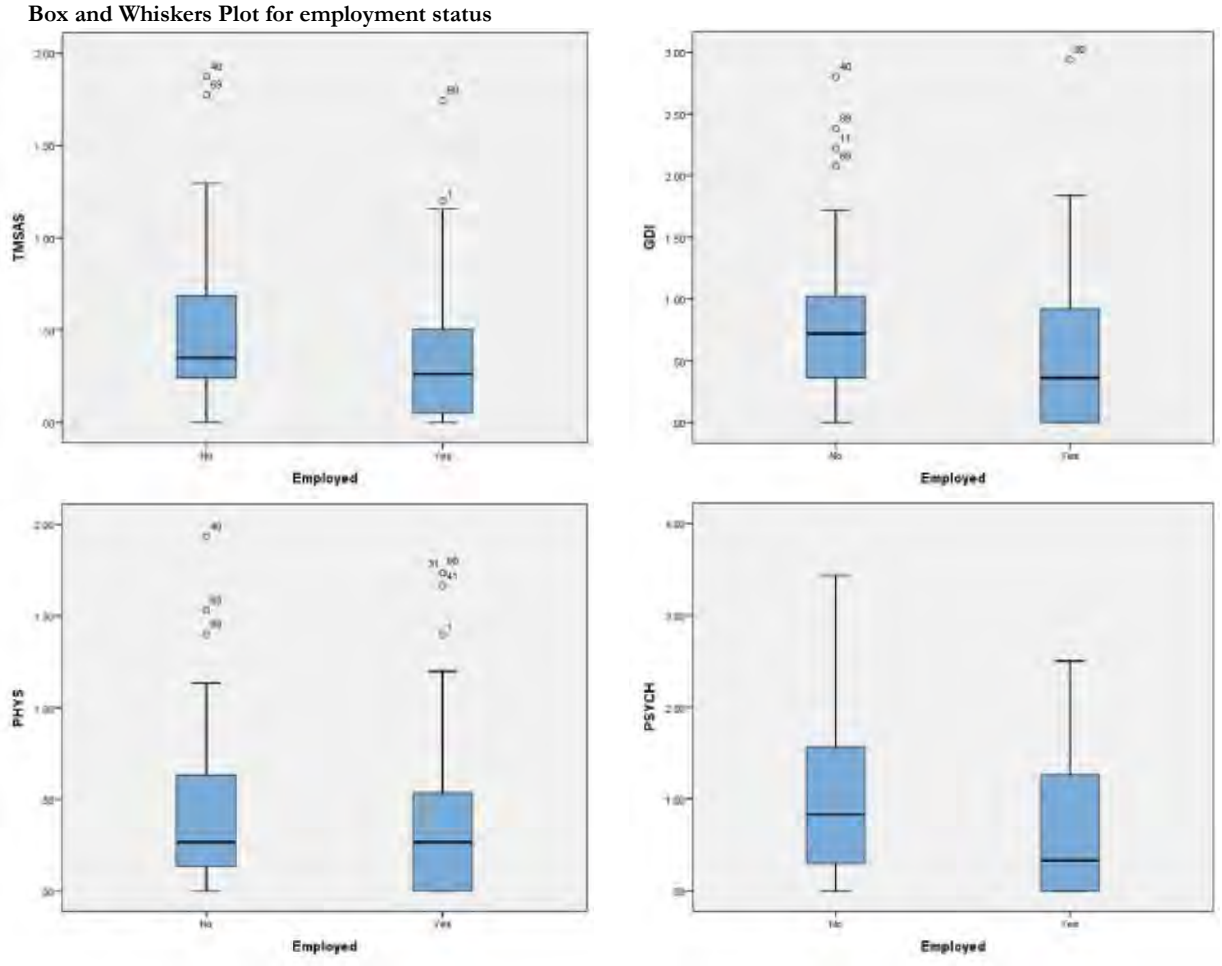
The association with type of HAART regime was not tested; the high number of different regimes amounts to very small sample sizes. Most of the regimes prescribed are no longer part of the recommended first line regimes according to the new local guidelines. Median values of TMSAS, GDI and PSYCH were significantly different between employed/unemployed (Figure 3), between males and females (Figure 4) and PHYS significantly different between males and females. There was no association with the CD4 count (Figure 5). Time on treatment is not significantly related to any of TMSAS, GDI, PHYS or PSYCH scores, but younger age was related to higher GDI (Table 6).

Box and whiskers plots in Figures 3 to 5 diagrammatically present the associations of employment status, gender, and CD4 count with the symptom indices. The bottom and the top of the boxes are

the first and third quartiles, while the band inside the box represents the median. The ends of the whiskers represent the lowest value still within 1.5*IQR (interquartile range) of the lower quartile, and the highest value still within 1.5*IQR of the upper quartile. Any data not included between the whiskers is plotted as an outlier with a numbered small circle, the number representing the number of the study participant.

Figure 3: Association of employment status with symptom indices

		Employed							
		Valid N	Minimum	Maximum	Mean	Standard Deviation	Median	Percentile 25	Percentile 75
TMSAS	No	35	.00	1.88	.53	.46	.35	.22	.70
	Yes	69	.00	1.74	.37	.37	.26	.05	.51
GDI	No	35	.00	2.80	.86	.72	.72	.32	1.06
	Yes	69	.00	2.94	.58	.62	.36	.00	.92
PHYS	No	35	.00	1.93	.46	.46	.27	.13	.67
	Yes	69	.00	1.73	.36	.44	.27	.00	.53
PSYCH	No	35	.00	3.43	1.09	1.03	.83	.27	1.60
	Yes	69	.00	2.50	.66	.74	.33	.00	1.27

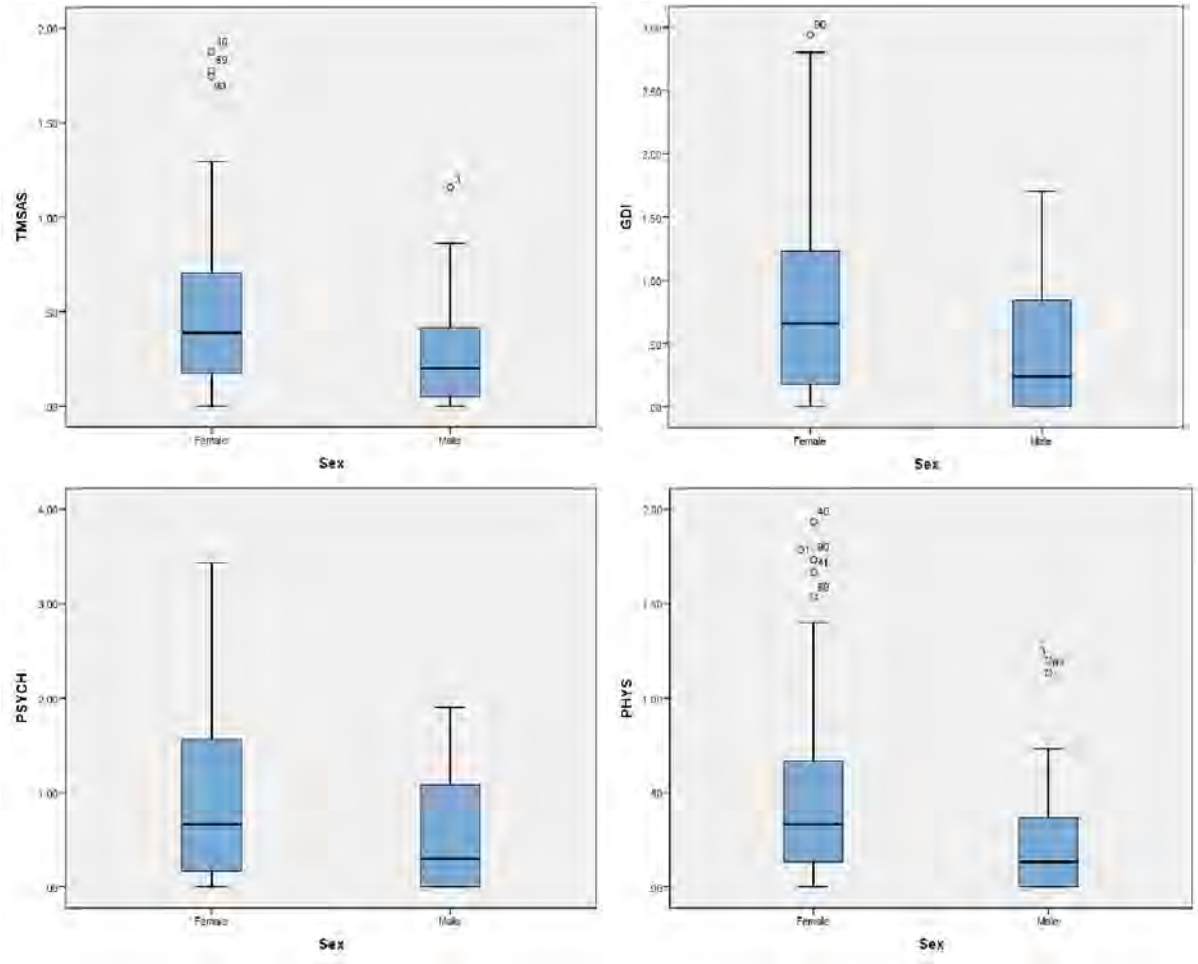


TSMAS, GDI and PSYCH are significantly increased in the unemployed

Figure 4: Association of gender with symptom indices

		Gender							
		Valid N	Minimum	Maximum	Mean	Standard Deviation	Median	Percentile 25	Percentile 75
TMSAS	Female	64	.00	1.88	.51	.45	.39	.17	.70
	Male	40	.00	1.16	.28	.26	.20	.05	.42
GDI	Female	64	.00	2.94	.81	.72	.66	.18	1.23
	Male	40	.00	1.70	.46	.50	.24	.00	.84
PHYS	Female	64	.00	1.93	.49	.50	.33	.13	.67
	Male	40	.00	1.20	.25	.30	.13	.00	.37
PSYCH	Female	64	.00	3.43	.96	.96	.67	.17	1.57
	Male	40	.00	1.90	.56	.62	.30	.00	1.08

Box and Whiskers Plot for gender

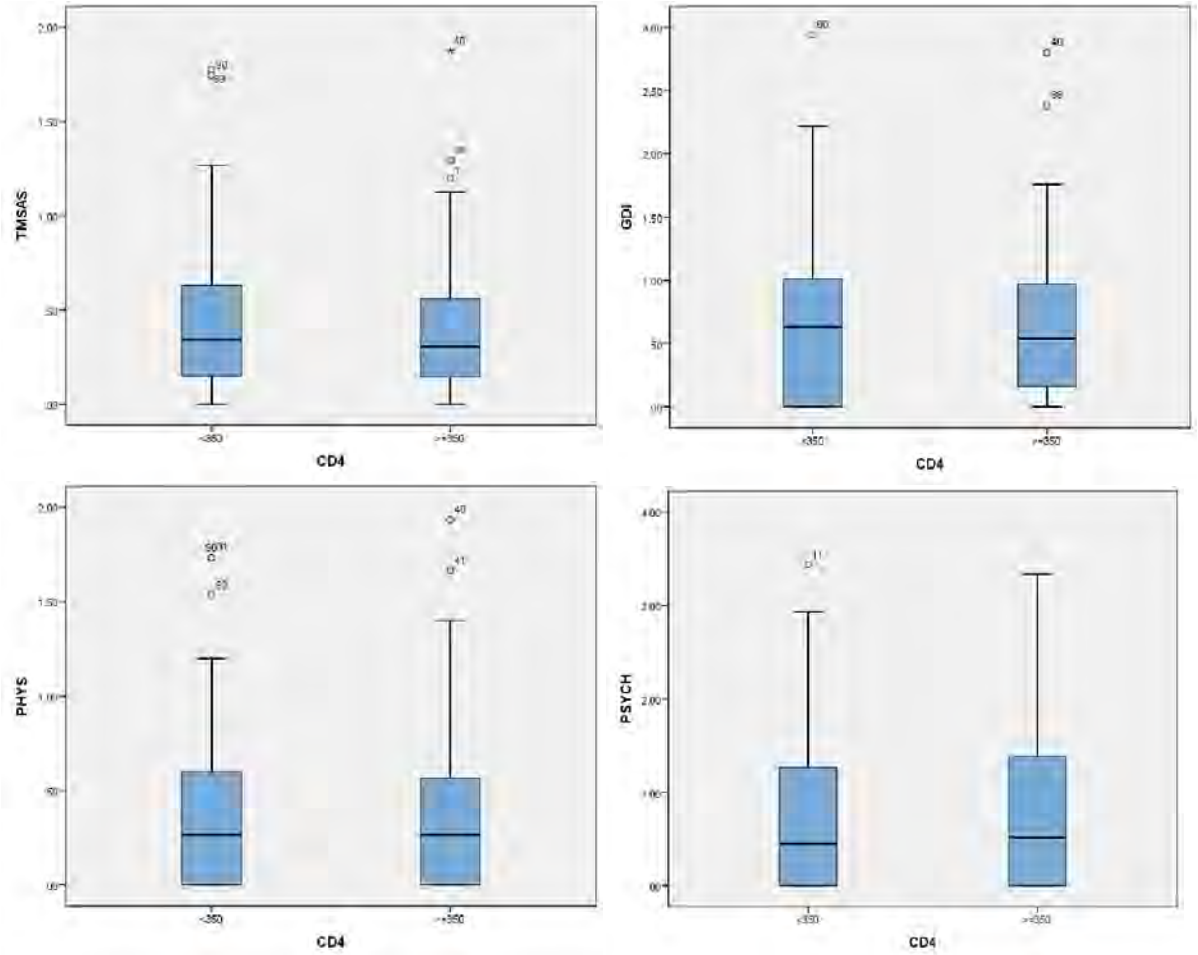


All 4 MSAS scores are significantly higher in female patients

Figure 5: Association of CD4 count with symptom indices

		CD4							
		Valid N	Minimum	Maximum	Mean	Standard Deviation	Median	Percentile 25	Percentile 75
TMSAS	<350	40	.00	1.77	.45	.45	.34	.15	.63
	>=350	64	.00	1.88	.40	.38	.31	.14	.56
GDI	<350	40	.00	2.94	.73	.73	.63	.00	1.01
	>=350	64	.00	2.80	.63	.62	.54	.16	.97
PHYS	<350	40	.00	1.73	.44	.48	.27	.00	.60
	>=350	64	.00	1.93	.36	.42	.27	.00	.57
PSYCH	<350	40	.00	3.43	.80	.92	.45	.00	1.27
	>=350	64	.00	3.33	.81	.84	.52	.00	1.38

Box and Whiskers Plot for CD4 count



There is no association between CD4 count and MSAS scores

Table 5: Null Hypotheses for the associations of MSAS scores with gender, employment status and CD4 count

Variable	By	Test Statistic	p	Conclusion
TMSAS		7.5	0.006	Reject H0
GDI		6.393	0.011	Reject H0
PHYS		7.367	0.007	Reject H0
PSYCH	Gender	5.137	0.023	Reject H0
TMSAS		4.098	0.043	Reject H0
GDI		4.43	0.035	Reject H0
PHYS		1.948	0.163	Do not reject H0
PSYCH	Employed	4.799	0.028	Reject H0
TMSAS		-0.13	0.896	Do not reject H0
GDI		-0.393	0.694	Do not reject H0
PHYS		-0.752	0.452	Do not reject H0
PSYCH	CD4	0.464	0.643	Do not reject H0

Table 6: Associations of time on treatment and age with symptom indices

Correlations								
			Age	Months on Rx	TMSAS	GDI	PHYS	PSYCH
Spearman's rho	Months on Rx	Correlation Coefficient		1.000	.038	.081	.003	.122
		Sig. (2-tailed)			.701	.857	.977	.219
		N		104	104	104	104	104
	age	Correlation Coefficient	1.000		-.131	-.200*	-.146	-.088
		Sig. (2-tailed)			.183	.042	.140	.376
		N	104		104	104	104	104
**. Correlation is significant at the 0.01 level (2-tailed). Younger Patients have a higher GDI								

Correlation between symptom reporting during follow-up and during the study

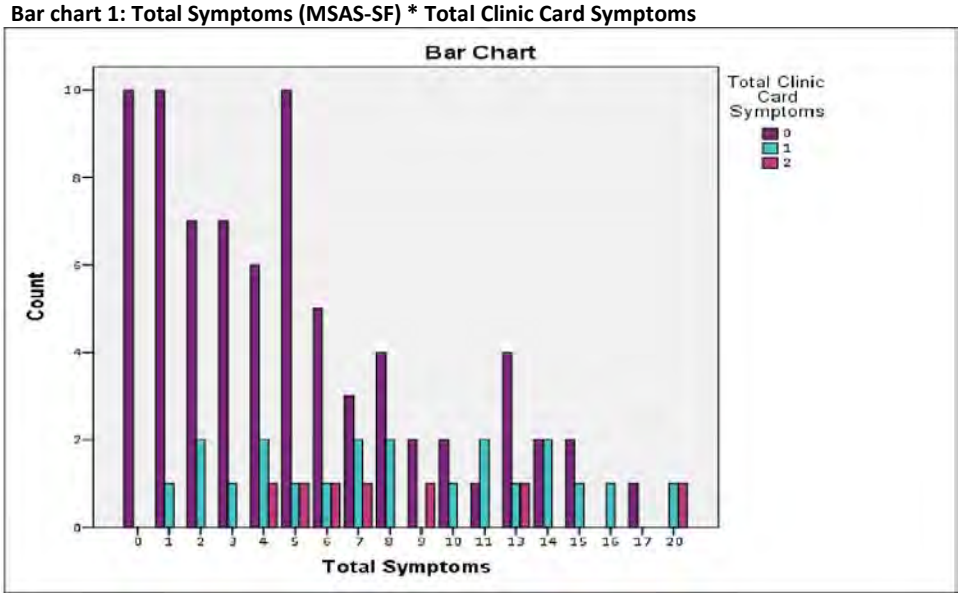
Participants of the study reported between zero and twenty symptoms according to the MSAS-SF questionnaire (Table 2). When collecting information from notes made in the patients' clinic cards during follow-up visits dating back 3 months and including the study day visit, the maximum number of complaints noted was two. Cough and pain were the most commonly reported symptoms during follow-up. Other recorded symptoms were pruritus, mouth sores, diarrhoea, loss of appetite, lack of energy and oedema. For 10 of the 28 reported pain complaints no treatment was recorded.

Paracetamol and Ibuprofen were the most commonly prescribed analgesics; one patient received Codeine and another Tramadol. None of the patients complaining of cough were known asthmatics or previously diagnosed with TB. Higher symptom burden as assessed by the MSAS-SF did not correlate with higher symptom reporting during clinic visits (Table 7).

Table 7: Total Symptoms (MSAS-SF) * Total Clinic Card Symptoms Cross tabulation

	Count	Total Clinic Card Symptoms			Total
		0	1	2	
Total Symptoms MSAS-SF	0	10	0	0	10
	1	10	1	0	11
	2	7	2	0	9
	3	7	1	0	8
	4	6	2	1	9
	5	10	1	1	12
	6	5	1	1	7
	7	3	2	1	6
	8	4	2	0	6
	9	2	0	1	3
	10	2	1	0	3
	11	1	2	0	3
	13	4	1	1	6
	14	2	2	0	4
	15	2	1	0	3
	16	0	1	0	1
	17	1	0	0	1
	20	0	1	1	2
Total		76	21	7	104

Bar chart 1: Total Symptoms (MSAS-SF) * Total Clinic Card Symptoms



Part 2: General practitioners

Sample characteristics

Requests to participate were emailed to all of the 35 general practitioners working in the Erongo region, of which 25 responded; 15 from the private and 10 from the public sector.

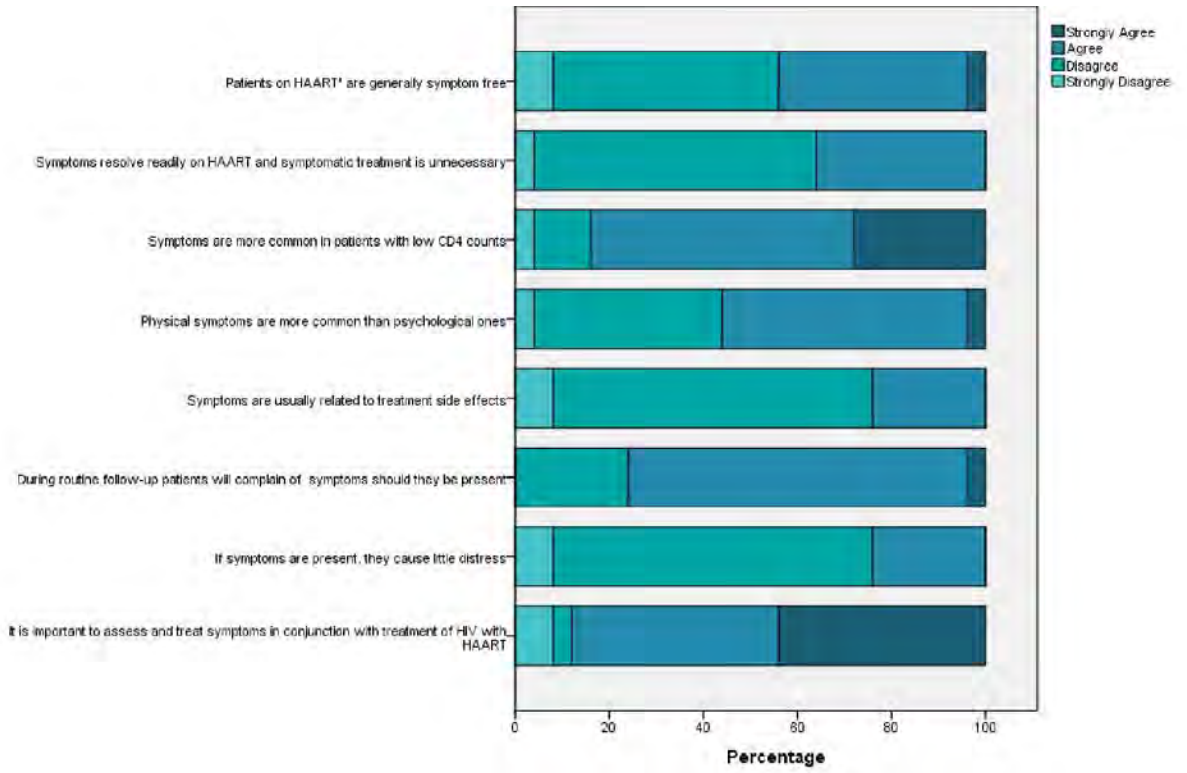
General practitioners' opinions (Table 8)

The majority (88%) of participants agreed that symptom assessment and treatment is important alongside treatment with HAART, 84% believed symptoms to be more common in patients with low CD4 count. Physical symptoms were thought to be more common (56%) and only 25% felt that symptoms, when present, caused little distress. Symptoms were not generally ascribed to treatment side effects and HAART was not expected to readily resolve symptoms and make symptomatic treatment unnecessary; almost half (44%), however, believed patients on HAART to be generally symptom free. The majority (76%) believed that patients would voice their symptom complaints during routine follow-up.

Table 8: General Practitioners' opinions

	Strongly disagree/disagree		Agree/Strongly agree	
	N	**%**	N	**%**
Patients on HAART are generally symptom free	14	**56**	11	**44**
Symptoms resolve readily on HAART and symptomatic treatment is unnecessary	16	**64**	9	**36**
Symptoms are more common in patients with low CD4 counts	4	**16**	21	**84**
Physical symptoms are more common than psychological ones	11	**44**	14	**56**
Symptoms are usually related to treatment side effects	19	**76**	6	**24**
During routine follow-up patients will complain of symptoms should they be present	6	**24**	19	**76**
If symptoms are present, they cause little distress	19	**76**	6	**24**
It is important to assess and treat symptoms in conjunction with treatment of HIV with HAART	3	**12**	22	**88**

Bar chart 2: General practitioners' opinions:



As clinicians in the public service see a lot more PLWHIV than private practitioners do, the assumption was made that their respective opinions would differ. In the current small sample, however, that did not seem to be the case (Table 9).

Table 9: Public versus private practitioner opinions

	Public (N=10)		Private(N=25)	
	Strongly disagree/ disagree	Agree/ Strongly agree	Strongly disagree/ disagree	Agree/ Strongly agree
Patients on HAART are generally symptom free	8	2	6	9
Symptoms resolve readily on HAART and symptomatic treatment is unnecessary	8	2	8	7
Symptoms are more common in patients with low CD4 counts	1	9	3	12
Physical symptoms are more common than psychological ones	6	4	5	10
Symptoms are usually related to treatment side effects	7	3	12	3
During routine follow-up patients will complain of symptoms should they be present	1	9	5	10
If symptoms are present, they cause little distress	9	1	10	5
It is important to assess and treat symptoms in conjunction with treatment of HIV with HAART	2	8	1	14

Table 10: Null hypotheses Public versus private practitioner opinions

Variable	Chi-Squared	d.f.	p	Fisher's p	Conclusion*
Patients on HAART* are generally symptom free	3.896	1	.048	.099	Do not reject H0
Symptoms resolve readily on HAART and symptomatic treatment is unnecessary	1.852	1	.174	.229	Do not reject H0
Symptoms are more common in patients with low CD4 counts	.446	1	.504	.626	Do not reject H0
Physical symptoms are more common than psychological ones	1.732	1	.188	.241	Do not reject H0
Symptoms are usually related to treatment side effects	.329	1	.566	.653	Do not reject H0
During routine follow-up patients will complain of symptoms should they be present	1.791	1	.181	.345	Do not reject H0
If symptoms are present, they cause little distress	1.791	1	.181	.345	Do not reject H0
It is important to assess and treat symptoms in conjunction with treatment of HIV with HAART	1.010	1	.315	.543	Do not reject H0

*no significant difference between public and private practitioners' opinions

In this chapter the symptom prevalence and burden of the study population was presented, as well as the health professionals' awareness of the plight of these patients. In the following discussion these results will be discussed in the context of the introduction and the literature review above.

Discussion

In this chapter the results are discussed following the headings used in the literature review; symptom prevalence and burden, effect of treatment, under-reporting and under-assessment of symptoms, barriers to symptom management and the need for palliative care will be discussed.

This was the first study to assess symptom experiences of patients living with HIV/AIDS in Namibia. The sample reflects the demographics of HIV infected patients accessing care in Namibia, being of a younger age group (average 39 years) and largely female (62%). In a recent review on the problem of pain in PLWHIV it was found that low-income countries and females were under-represented in the studies[48]. This study adds to the knowledge about the burden of symptoms in female and male patients living with HIV in developing countries.

Palliative care includes but goes beyond the medical management of HIV/AIDS. According to the WHO definition it improves the quality of life of patients and their families facing the problems associated with life-threatening illness, "through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosomatic and spiritual"[17]. Equally, quality of life not only depends on good clinical care, but involves non-health related issues such as addressing poverty, stigma, gender equity, nutrition, sanitation, and housing and clean water supply. Symptom management is only a part of holistic patient care. This study on prevalence of symptoms emphasises the need for comprehensively addressing symptoms and suffering throughout the continuum of HIV disease as a first step towards holistic patient care.

Symptom prevalence and burden

Despite apparently normal functioning, patients coming for routine follow-up treatment were found to have a high 7 day symptom prevalence in the current study population on HAART; an average of 6 out of possible 32 symptoms were reported. In the pre-HAART era Breitbart et al[10,34] described that the presence of pain was associated with the number of concurrent symptoms, and in this study the average of symptoms present was 9 in those study participants who reported pain.

As in many other studies[43,53] psychological symptoms as well as pain are highly prevalent and cause for distress. Pain decreases quality of life; it is associated with increased psychiatric disease[43,26]; it is associated with sleep disturbance and fatigue[36,63]. These associations alone may explain the presence of the ten most commonly reported symptoms in this study, excluding peripheral neuropathy and cough: the psychological symptoms (worry, feeling sad, irritable and nervous) as

well as pain, difficulty in concentrating and sleeping and lack of energy. So by properly assessing and managing pain, symptom burden can be reduced and quality of life improved.

Harding and Sherr[49] reported that symptom burden does not only influence quality of life, it also is associated with poor treatment adherence, treatment switching, sexual risk taking and viral rebound. High symptom burden that remains unaddressed might lead to self-care strategies that are harmful or ineffective[63]. Patients tire of side effects of treatment which might lead to non-compliance[16]. This is why the Namibian HIV treatment guidelines[31] should emphasise symptom assessment and management much more clearly than only advising to be on the look-out for medication side effects, opportunistic infections and disease progression. Other than peripheral neuropathy and cough none of the common symptoms are obviously disease or treatment related, but they are still intricately linked to disease management.

Cough and pain were reported most common physical symptoms reported in this study. Despite cough being reported in combination with sweats and/or chest pain, there was no indication in the clinic cards that these patients were investigated for TB. This constitutes missed opportunities to diagnose TB and to prevent the increased morbidity associated with late diagnoses and possible drug resistance.

Women and unemployed patients had significantly higher distress as measured by the MSAS-SF subscales TMSAS, PSYCH and GDI. Females also suffered higher physical symptom distress, whereas younger patients had significantly higher global distress indices. More than half of the women participants were under the average age of the study population. Women also comprised most of the unemployed. The higher distress in the younger patients, the unemployed and in females is thus interlinked. The higher global burden amongst the younger patients could also result from being more educated, more outspoken and less fatalistic with regards to their disease. Fatalism is one of the concerns addressed in the Barriers Questionnaire designed by Ward et al[83] when investigating patient barriers to symptom reporting. This might be that less evident in young adults; especially young females, who not only have their own lives ahead of them but also have to think of their young children's future. These young women might be less willing to accept symptoms that remind them of their chronic disease and will not resort to passive acceptance. However, poor coping skills and little emotional, psychological or spiritual support will lead to increased physical and psychological morbidity[5]. Lack of energy, one of the symptoms making up the physical component of the GDI, was commonly reported high distress symptom and might also be felt more acutely in the younger population.

This study confirms the finding of many other studies[10,63,84] that women experience a higher symptom burden and have also been shown to risk non-adherence to treatment in order to avoid side effects[62]. A study by Breitbart[85] showed that women and poorly educated patients are more likely to receive inadequate pain control. If symptoms are not addressed and are interpreted as treatment side effects this might lead to inadequate disease control. Women constitute thus a very vulnerable population and increased attention is required toward relieving their plight.

Although not investigated as part of this study, symptom burden may be expected to be higher in the rural and poorer areas of Namibia, where unemployment and poor education are a bigger problem than in urban areas. Mothers often stay alone with their children in the rural homes and the chronically ill usually migrate back to these homes. Distances to the nearest clinic and to any pharmacy for self-medication are greater.

Breitbart el al[10] were the first to use the MSAS-SF to measure symptom prevalence and burden in AIDS patients. In their study the internal consistency of the subscales of the MSAS-SF was as high in that AIDS population as it was in cancer populations[33]. Since the advent of HAART symptom prevalence is still high, but the profile of prevalent symptoms that end stage cancer patients and AIDS patients had in common, has changed. Even though the MSAS-SF has been extensively used to collect data amongst patients with less advanced HIV disease on ART and in studies in sub-Saharan Africa, it has never been validated for these populations. High distress symptoms such as peripheral neuropathy, problems with sexual function/activity, body image, sleeping and concentration difficulties are not included in scales used to calculate global burden and physical distress. Different cultures might interpret and experience symptoms differently. In a study done in Uganda[52] additional distressing symptoms were identified, such as hunger and difficulties with moving/walking. The physical symptom distress score as well as the global symptom distress index might differ if these respective distressful symptoms were included in the calculations.

The APCA-POS, which is a core outcome measure for palliative care in Africa, assesses physical and psychological symptoms, spiritual, practical and emotional concerns and psychosocial needs of the patient and family[76]. Despite it addressing palliative care needs to a much greater extent than the MSAS-SF, the latter was chosen for this study because of more detailed symptom assessment. The APCA-POS is used for clinical audits and for measuring outcomes of improvements made to existing palliative care. This study attempted to create an awareness of the symptom burden amongst PLWHIV. Impeccable symptom control is a start towards improving patients' quality of life and should be a routine part of patient care.

Irrespective of the above concern it has been shown without doubt internationally and locally that patients living with HIV have a high symptom burden, and that the issue at hand now is to improve symptom assessment and management[50].

Symptoms: Treatment or disease?

Efavirenz/Emtrictabine (or Lamivudine)/Tenofovir is now the preferred regime in treatment naïve HIV patients internationally[12] and locally as endorsed by the 2014 Namibian national guidelines[31]. It has been shown to achieve and maintain viral suppression whilst having a good tolerability profile. Symptoms such as peripheral neuropathy, nausea and vomiting, loss of appetite, abnormal taste of food, skin problems and abdominal discomfort were significantly less than with other HAART regimes[12]. Lamivudine (3TC) and Emitricabine (FTC) are pharmacologically similar and are clinically interchangeable[86]. 3TC has a shorter intracellular half-life than FTC, but it was shown that this did not lead to a significant increase in resistant HIV mutations[87]. However, only FTC is available in a fixed dose combination (FDC) with Tenofovir (TDF) and Efavirenz (EFV), which makes it the more favourable drug to use.

It is a concern that despite national guidelines, the study participants were on 8 different treatment regimes; the most commonly prescribed HAART was TDF/3TC/NVP; only 20 % were on the recommended treatment regime. It is of concern that there are still patients receiving Stavudine, despite the recent 2014 guidelines[31] strong recommendation to eliminate D4T based regimes. The previous 2010 Namibian national guidelines[88] already warned against the well documented long-term side effects, such as lipodystrophy, peripheral neuropathy and lactic acidosis. The guidelines also recommend that patients on AZT, NVP or D4T based regimes are identified and changed to the now available FDC formulation. Of the 76 study participants eligible for such a change provided they had sufficient viral suppression, only 29 had recent viral loads available; of these only 3 were sufficiently suppressed.

This study confirms that even while well and on ART, PLWHIV experience many symptoms. This was also reported in an online survey amongst gay men living with HIV in the UK[35], where the mean total number of symptoms was 14 for those on HAART and 10.3 for those not on ART. In the UK study psychological distress was the same for both groups, but PHYS scored higher in patients on HAART, although, as in the current study, the subscale scored less than one. HAART users had more pain, lack of energy, drowsiness and peripheral neuropathy; the latter two being known side effects of Efavirenz, Didanosine and Stavudine. The UK and the current Namibian study clearly showed that

HAART does not eliminate the symptom problem in PLWHIV, but optimal choice of treatment regimes can prevent unnecessary symptoms due to treatment side effects.

Starting ART once the CD4 level is below 500 instead of the previous value of 350 was introduced locally in 2014. With an average CD4 count of 444 and 40% of study participants having a CD4 count of less than 350, the immune status is relatively low. Looking at these CD4 counts and corresponding treatment regimes, there seems to be a reluctance to change to second line treatment which could indicate that there are patients with undiagnosed treatment resistance which might lead to increased infectivity, morbidity and mortality. It is important that the recommended viral load measurements are adhered to and acted upon, in order to diagnose and treat insufficient viral suppression.

Under-recognition and under-reporting of symptoms/ barriers to symptom control

There was a big discrepancy between the symptom prevalence as assessed by patient self-report by direct questioning using the MSAS-SF and the prevalence as reported in the clinic cards by the health care professionals during normal follow-up visits. The majority (90%) of patients reported at least one symptom in the questionnaire, the overall prevalence ranging from 0 to 22. Of these patients only 50 (48%) had symptoms recorded during follow-up visits, the maximum number of symptoms recorded being 2; although as discussed earlier the average number of symptoms identified by patients was 6. It is possible that the specific HAART records that are kept at the clinic have details that were not transferred to the clinic cards, but that alone would not explain the large disparity. It is clear that symptoms were not actively assessed.

Patient-related barriers to reporting pain in cancer[83] and AIDS patients[41] could explain some of this disparity. Fear of distracting health care providers from treating the disease, interpreting symptoms as signs of disease progression, fear and concern about side effects and pill burden, inadequate communication[72] as well as fatalism have been described as factors preventing patients from reporting symptoms[41].

During the pilot study it was clear that patients were reluctant to communicate symptoms to a familiar clinic sister. Despite using an unfamiliar research nurse in a separate room in the clinic for completing the questionnaires, the clinic as well as the community is small enough to know everybody else and watch their movement, so that some might have felt that privacy was not enough[73]. The symptom report during normal follow-up visits, as recorded in the clinic cards, in comparison to those reported in the questionnaire is also an indication of the reluctance to report

problems if not directly asked about symptoms. When designing the study the HIV clinics were not yet run by nurses and patients had a long wait until they got seen by the medical officers. That time was designated for filling in the questionnaire. When the data collection was started, the clinic had become a nurse-run clinic, waiting times were drastically improved and patients were reluctant to "waste time" and might not have taken the time to think about the questions and reported no symptoms in order to get home or back to work faster.

It is known that open ended questions are less sensitive in eliciting symptoms and that patients are more likely to recall symptoms when prompted with a list[61]. A symptom check list that could be completed by the patient with or without the help of the health care provider would empower the patients to overcome a lot of the possible barriers to reporting symptoms and would assist health care providers with symptom assessment.

Under-estimation and under-treatment of symptoms by health care providers is a well known fact[39,40,65]. Symptoms are often under-recognised either because health care providers do not ask, focus on the treatment of the disease only[68] or consider them "subclinical"[13]. The health care providers in this study were all aware of the need for assessment and management of symptoms alongside HAART; most of them also knew that symptoms could be distressing and would not disappear readily by using HAART. However, 44% believed HIV patients to be generally symptom free. No other study could be found where it was made explicitly clear that health care providers assume that patients would report symptoms when present. Breitbart et al[41,71] found that most clinicians, except for those with more knowledge regarding pain management, do not see patient under-reporting as a barrier to pain management. Increasing health professionals' skills in symptom assessment and management as well as creating awareness about patients' barriers to symptom reporting would improve patients' quality of life.

The majority of health care providers in this study associated high symptom prevalence with a low CD4 count. Even in the pre-HAART era, no association was found between CD4 count and symptom burden[33]. Fontaine et al [66] found that physicians' recognition rates of symptoms were better in sicker patients, probably because they are expected to be symptomatic.

Resnik et al[68] showed that clinical assessment is more likely to focus on disease and markers of disease management than on patients' personal experiences. Despite knowing that symptoms are not just due to medication side effect, there is little indication in this study that ANY symptoms were actively sought for. Other symptoms that were commonly reported in the MSAS-SF and could have been due to side effects or disease progression /opportunistic infections, such as peripheral

neuropathy, itching, bloatedness, dry mouth, sweats and drowsiness were not reported and hence not assessed for.

The advantages of nurse initiated HAART are faster and more available services, especially in rural areas where availability of doctors is limited. Nurses, however, are not medically trained in symptom control, diagnoses and management of other diseases. This might lead to under-recognition of symptoms and symptom aetiology, limited symptomatic control and late diagnoses of co-morbid conditions. Palliative care nurses are trained in symptom assessment and management and provide good total symptom control. The World Health Assembly resolution suggests that all health care providers should be trained in palliative care[22]. Integrating palliative care training into the nurse initiated HAART training would empower nurses to provide a better service, would benefit all patients attending HAART clinics in the country and would be a first practical step for the Namibian government to take to introduce palliative care into their health system.

The danger of identifying PLWHIV as asymptomatic is the failure to recognise a cluster of symptoms that when managed appropriately could improve quality of lives[13] and treatment adherence. Wrong assumptions, such as "patients on HAART being symptom free", "patients will report symptoms if present" and that "high CD4 counts protect from symptoms" lead to poor symptom assessment.

Many practitioners had no formal training in HIV management or in palliative care. A strong case is made that such topics should be included in Continuous Medical Education programs and that stricter protocols are made available. Other studies[38,15] also found provider recognition of symptoms poor and made a case for tools to be implemented to improve symptom recognition and management.

Ward et al[83] stressed the importance of good communication and addressing concerns in cancer patients before patients complain. The same should apply to PLWHIV. The importance of reporting symptoms and other problems should be part of every HAART initiation discussion. Many patients on HAART have presented initially with advanced AIDS and will have experienced dramatic improvements in well-being, which might make them tolerate symptoms rather than voice them. Patients should be informed that they will not be symptom free immediately when starting HAART, but that most symptoms can be treated effectively and it should be encouraged that non resolving symptoms need to be reported.

Limitations of the study

Being unused to taking part in research, the study participants might have benefitted from a second research assistant for informing them about the study and discussing questions and doubts before

the questionnaire was administered. Equally, the health practitioner recorded symptoms might have been a bit more, if the HIV clinic records were reviewed and not only the cards carried by the patients. This would, however, not have influenced the conclusion, that symptom assessment by health care professionals and patient-reporting of symptoms is poor.

Only general practitioners and state employed medical officers were requested to fill in the health professionals' questionnaire. As the nurses now initiate the HAART and see patients for follow-up, they should have also been included. The data extracted from the clinic cards were mainly reported by nurses, so it is unlikely that their opinions differ a lot from those of the doctors as symptom assessment was poor, probably because the same incorrect assumptions were made.

Palliative care

Reported pain prevalence ranges from 50 to 67% throughout all stages of HIV disease[48]. In this study as in others[43,53] psychological symptoms and pain rate high amongst symptoms causing a lot of distress. The concept of "Total Pain" applies[17,86] in HIV medicine as is does for palliative care in general. PLWHIV as well as their families are confronted with many additional social and psychological problems besides the physical aspects of the disease[89]. Employment issues, finances, stigma, relationships and having to comply with care all influence the experience of pain. Kagee et al[55] showed in a study done in South Africa that psychological distress was equally high in patients with other chronic diseases such as hypertension and diabetes.

The approach to management of PLWHIV may be improved as in Tanzania[75] which shows that minimal basic palliative care training of the clinic staff providing standard HIV care, continuing support of staff and palliative care drug availability improved the quality of life of patients attending these HAART clinics significantly. Similar training and assurance of drug availability would improve symptom assessment and management and should have the same effect amongst the local HIV population. A greater presence of motivated social workers at the relevant clinics might aid in alleviating some of the problems that are common especially amongst impoverished communities

Even though medical officers working in the public health sector have a greater experience in treating HIV patients because of the greater number of patients, their perceptions and insights did not differ from general practitioners, who see fewer HIV patients, but theoretically have more time to spend exploring patient experiences. Private patients, who can choose their health care provider and can build up trust in a particular health care provider, might have fewer barriers to reporting symptoms. Good doctor-patient concordance regarding HIV treatment decision making and good communication results in better physical and psychological functioning[32]. Personalised treatment of

the disease and the total patient should be possible even in busy public hospital clinics. Even in the absence of a structured palliative care team or system, the assessment and treatment of pain and other distressing symptoms should be part of every doctor-patient interaction. Unaddressed physical and psychological symptoms have clinical implications as discussed above; leading to decreased treatment adherence and treatment failure with its consequences.

The first decade of the HIV disease trajectory in the USA was characterised by high mortality and morbidity due to opportunistic infections. With the introduction of ART in the early nineties mortality declined drastically. In this current chronic disease era, which is managed by HAART, the decline in mortality has levelled off. Morbidity and mortality are increasing again due to accelerated of diabetes, lipid disorders, cancers, generalised debility and treatment failure[4,90].

In Namibia HAART only became available for all 10 years later than in the USA. Patients still present with opportunistic infections and very low CD4 counts. There are many risk factors to poor adherence and considering the natural progression of disease and its co-morbidities, it is likely that a time will come, when, as in the USA, mortality will be on the increase again.

The 2014 World Health Assembly resolution on palliative care urges member states, of which Namibia is one, to integrate basic training and continuing education on palliative care "as a routine element of all undergraduate medical and nursing professional education, and as part of in-service training of caregivers at the primary care level, including health care workers, caregivers addressing patients' spiritual needs and social workers"[24].

As well as the benefits of providing palliative care focused on symptom management and psychosocial support, end-of-life care for HIV patients still is and always will be a reality and it is a matter of urgency that steps are taken to provide palliative care to all HIV and other patients in Namibia.

Conclusion

This study was the first in Namibia to investigate symptom prevalence and burden of HIV patients on HAART. It adds to the knowledge about the plight of HIV/AIDS patients in the less researched under developed countries.

All objectives of the study were achieved:

1) Symptom prevalence was high amongst the study population, psychological symptoms being by far the most common and distressing. In particular, young, unemployed, female patients reported high physical, psychological and global distress and special attention should be given to recognise the plight of this population group.
2) Despite high symptom prevalence as measured by the MSAS-SF, patients are reluctant to report symptoms during follow-up visits. Patient barriers to symptom report need to be identified and addressed.
3) Health care practitioners in the public and in the private health care sector agreed on the importance of good symptom assessment and management. However, quite a number assumed patients on HAART to be symptom free, that only a low CD4 count was associated with symptom burden and the majority assumed that patients would voice their symptoms.

It is clear that, as in other countries, PLWHIV have a high symptom burden and that these symptoms are not managed appropriately, mainly because of poor symptom assessment. The fact that patients do not voice their problems and that health care providers assume that they will do so thus being seen as symptom-free is a recipe for misunderstanding, poor symptom assessment and lack of management. Palliative care training of all health care practitioners managing HIV patients needs to be introduced to help patients live well with their disease.

Recommendations

A number of recommendations can be made based on the above findings:

1) Stricter adherence to treatment guidelines is recommended.
    i) Drugs, such as Stavudine, that are no longer recommended in standard treatment regimes should only be made available after special motivation by the prescriber.

ii) State pharmacy audits should be reviewed to see whether new treatment guidelines are adhered to.

iii) In private practice the control boards of the medical aid schemes, which previously had HIV advisors, should reintroduce review of prescribed medicines before authorising payments.

iv) Viral load monitoring should become a priority and systems need to be in place to ensure that failing treatment regimes are changed.

2) A symptom check list should be made available to PLWHIV when presenting for follow-up. Symptom assessment can be improved by providing such a check lists to patients. Patients find it easier to recall symptoms when presented with a list[59] and health care providers would be provided with a time saving list of symptoms to be addressed.

3) To better assess symptom prevalence and burden in the African context, the MSAS should be revised and validated for PLWHIV, especially for those living in Africa.

4) Symptom prevalence and burden is high in most patients with chronic illnesses[55]. It has been shown that even minimal palliative care training of nursing staff improves the quality of lives of PLWHIV[75]. Integrating palliative care training into nurse initiated HAART training, which could easily be extended to primary care nurses dealing with other chronic illnesses would be a start to providing palliative care in Namibia.

5) Continuous Medical Education programs for general practitioners in public and private services should include education about symptom assessment and management in PLWHIV.

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Appendices

Appendix 1 Memorial Symptom Assessment Scale – Short Form (MSAS-SF)

I) Instructions: Below is a list of symptoms. If you had the symptom DURING THE PAST WEEK, please check Yes. If you did have the symptom, please check the box that tells us how much the symptom DISTRESSED or BOTHERED you.

Check all the symptoms you have had during the PAST WEEK	YES	If YES: How much did it DISTRESS or BOTHER you? Not at All (0)	A little Bit (1)	Some-what (2)	Quite A Bit (3)	Very Much (4)
Difficulty concentrating						
Pain						
Lack of energy						
Cough						
Changes in skin						
Dry mouth						
Nausea						
Feeling drowsy						
Numbness/tingling in hands and feet						
Difficulty sleeping						
Feeling bloated						
Problems with urination						
Vomiting						
Shortness of breath						
Diarrhoea						
Sweats						
Mouth sores						
Problems with sexual interest or activity						
Itching						
Lack of appetite						
Dizziness						
Difficulty swallowing						
Change in the way food Tastes						
Weight loss						
Hair loss						
Constipation						
Swelling of arms or legs						
"I don't look like myself"						
If you had any other symptoms experienced during the PAST week, please list them below and indicate how much the symptom distressed or bothered you 1.						
2.						

II) Below are other commonly listed symptoms. Please indicate if you had the symptom DURING THE PAST WEEK, and if so, how OFTEN it occurred

Check all the symptoms you have had during the PAST WEEK	Yes	If YES, how often did it occur?			
		Rarely (1)	Occasionally (2)	Frequently (3)	Almost constantly (4)
Feeling sad					
Worrying					
Feeling irritable					
Feeling nervous					

Figure 1. Revised Memorial Symptom Assessment Scale Short Form [38]

Appendix 2

Demographic data

Date

Male/ Female Age

Employed: Yes / No

Last CD4

Last Viral Load Months on treatment

HAART regime: 1) _____

2) _____

3) _____

Other medication: 1) _____

2) _____

3) _____

Symptoms reported in clinic card: Treatment received:

1) _____

2) _____

3) _____

4) _____

5) _____

6) _____

7) _____

8) _____

Appendix 3

An investigation of the provision of holistic care to HIV patients in public and private health in Namibia

Dear Colleague

The above named study forms part of a requirement towards obtaining a Masters degree in palliative care.

Please assist me by taking the time to fill in the questionnaire below. There are no right or wrong answers. This is an attempt to compare health professionals' perception of the presence of symptoms in HIV patients to the perceived symptoms of the patients themselves.

Questionnaire:

Please cross the appropriate box:

State Service: ☐ Private Practitioner: ☐

	Strongly disagree 1	Disagree 2	Agree 3	Strongly agree 4
Patients on HAART* are generally symptom free				
Symptoms resolve readily on HAART and symptomatic treatment is unnecessary				
Symptoms are more common in patients with low CD4 counts				
Physical symptoms are more common than psychological ones				
Symptoms are usually related to treatment side effects				
During routine follow-up patients will complain of symptoms should they be present				
If symptoms are present, they cause little distress				
It is important to assess and treat symptoms in conjunction with treatment of HIV with HAART				

*HAART= highly active antiretroviral treatment

Appendix 4

Information Sheet for:

An investigation of the provision of holistic care to HIV patients in public and private health in Namibia

Thank you for giving your time to hear about our study:

What is the purpose of the study?

Patients living with HIV have a lot of problems. We want to find out what health complaints people on HIV treatment have. We also want to find out whether they voice these complaints to their health care professionals and whether they are heard.

Do I have to take part?

Taking part is completely voluntary and you decision will NOT affect you care in ANY WAY. If you agree to take part you will be asked to sign a consent form to show that you wanted to take part. You can change your mind at any stage.

What will happen when I take part?

A researcher and a clinic nurse will ask you questions about the presence of pain or other symptoms you may have. At the same time we will investigate whether these complaints have been addressed by reading notes made in your clinic card.

Benefits of the study

There are no personal benefits to the study, but it might encourage you to voice your problems. The information you provide may help create awareness about what problems patients living with HIV do have.

Disadvantage

Although unlikely, some questions may make you feel sad or distressed. Should that happen, we will try and arrange time with a counsellor for you.

Will my taking part in the study be kept confidential?

All the information which we collect during the interview will be kept strictly confidential. Your personal details (for example name and address) will be kept separately from the information you give. We will use a number and not your name on any information you give us. No-one outside the study will have access to the information you give us.
For patients in this study we will record their illness. That information will be treated as confidentially as all the other information you give us, and no-one outside this study will be able to find out your name or any other information that would identify you.

How will I know about the results of the study?
At the end of the study the results will be displayed on a poster at the clinic.

Who is organizing the research?
If you have any questions or need to talk to anyone about this research, you can contact the people listed below. Thank you for thinking about taking part in the study.

If you have any questions about the study, contact:

Dr Maja Brand, Swakopmund: Tel 429000

If you have any questions about your human rights of any ethical issues about the study:
UCT Research Ethics Committee:
Mrs Lamees Emjedi: Telephone: 0027-21- 406 6338

Appendix 5

Consent Form for

An investigation of the provision of holistic care to HIV patients in public and private health in Namibia

1. I confirm that I have read and understand the information sheet and have had the opportunity to ask questions.

2. I understand that my participation is voluntary and I am free to withdraw at any time, without giving a reason, without my care being affected.

3. I agree to take part in the above study.

Name _____

Signature _____ Date _____

Researcher: Signature _____ Date: _____

Witness: Name
(from clinical team or family member)

Signature _____ Date: _____

Appendix 6

UNIVERSITY OF CAPE TOWN

Faculty of Health Sciences
Human Research Ethics Committee
Room E52-24 Groote Schuur Hospital Old Main Building
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
e-mail: shuretta.thomas@uct.ac.za
Website: www.health.uct.ac.za/research/humanethics/forms

22 July 2013

HREC REF: 328/2013

Dr M Brand
c/o Dr L Gwyther
Public Health & Family Medicine
Falmouth Building

Dear Dr Brand

PROJECT TITLE: AN INVESTIGATION OF THE PROVISION OF HOLISTIC CARE TO HIV PATIENTS IN PUBLIC AND PRIVATE HEALTH IN NAMIBIA

Thank you for your response to the Faculty of Health Sciences Human Research Ethics Committee received on 18th July 2013

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year till the 30th July 2014

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/research/humanethics/forms)

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please quote the HREC. REF in all your correspondence.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN ETHICS
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.
The Human Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

s.thomas

Appendix 7

9 - 0/0001

REPUBLIC OF NAMIBIA

Ministry of Health and Social Services

Private Bag 13198 **Ministerial Building** **Tel: (061) 203 2560**
Windhoek **Harvey Street** **Fax: (061) 222558**
Namibia **Windhoek** **E-mail:** tkakili@yahoo.com
Enquiries: Ms. T. Kakili **Ref:** 17/3/3 **Date:** 04 September 2013

OFFICE OF THE PERMANENT SECRETARY

Dr Maja Brand
P.O. Box 2680
Swakopmund

Dear Dr Brand

Re: An investigation of the provision of holistic care in private and public health in Namibia.

1. Reference is made to your application to conduct the above-mentioned study.

2. The proposal has been evaluated and found to have merit.

3. Kindly be informed that permission to conduct the study has been granted under the following conditions:

3.1 The data to be collected must only be used for the completion of your Maters degree in Palliative Medicine;
3.2 No other data should be collected other than the data stated in the proposal;
3.3 A quarterly report to be submitted to the Ministry's Research Unit;
3.4 Preliminary findings to be submitted upon completion of study;
3.5 Final report to be submitted upon completion of the study;
3.6 Separate permission should be sought from the Ministry for the publication of the findings.

Yours sincerely,

MR. ANDREW NDISHISHI
PERMANENT SECRETARY

"Health for All"

Appendix 8

Letter to local facility

Dr M. Brand

P.O. Box 2680

Swakopmund

Tel. 064-429000

The Chief Medical Officer

Erongo District

Private Bag

Swakopmund

29.4.2013

Dear Dr Musasa

An investigation of the provision of holistic care to HIV patients in private and public health in Namibia

Following a discussion we had earlier, I am now writing to invite the HIV/HAART clinic of the Swakopmund hospital to join us as a study site in our research.

The research is part of a Master's thesis in palliative care. Palliative care is the care of patients with life threatening illnesses and focuses on relieving and preventing suffering and improving quality of life. Patients living with HIV are known to have a high symptom burden and this study aims to assess that burden in the Swakopmund study population and to compare it to the awareness of healthcare professionals in Namibia and to the corresponding treatment provided.

This study is a cross-sectional study to assess the prevalence of symptoms and the associated burden in patients using HAART. The Memorial Symptom Assessment Scale will be used. It is a patient rated instrument that has been used in many studies, including sub-Saharan Africa to assess prevalence and burden of multiple symptoms in patients with medical illnesses.

The study received ethical approval from the Namibian ethical committee, ref. nr.: , as well as the University of Cape Town Faculty of Health Sciences Human Research Ethics Committee, ref. nr: .
Your staff will be fully briefed about the study before commencing.

Below an outline of some basic study information:

- Who will be recruited?

A total of 96 adult patients on HAART attending the HIV clinic on the agreed upon study days will be recruited

- How will patients be approached to ask them to take part?

We will ask your staff to identify patients that meet the criteria. Then an explanation will be given that we would like to recruit patients to a study that uses a questionnaire to ask questions about their health. This will involve a once off interview and will take about 20 minutes of their time. Interested patients will then be given more information by the researcher and asked to sign consent.

- How will data collection happen?

The researcher will then conduct the interview if the patient has given consent. The researcher will hold and store the data in a locked store and will keep the personal information (e.g. name) separate from the questionnaire data. The patient's name will not appear on the questionnaire which will only have a study number as an identifier.

- Responsibilities of the study site

We are asking you to assist in identifying patients who meet the study criteria and to introduce them to the researcher who will discuss the research with them and ask for their informed consent. We are also asking that should a patient become distressed during the interview that your counselling staff would be prepared to provide the necessary support for the participant. We have found in previous studies that participants welcome the opportunity to respond to questions asked in the Memorial Symptom Assessment Scale and that distress is infrequent. Please would you note your agreement to provide this support when you respond to our request to conduct research within your facility.

- Study feedback

Pertinent results will be made available to the study population in lay language in the form of a multilingual poster to be displayed at the local HIV clinic. More detailed scientific abstract will be made available to all healthcare professionals and the full thesis send to the Ministry of Health.

I will be the principal investigator throughout the study. Please do not hesitate to contact me should there be any queries at any stage of the study. I am looking forward to work with you and your staff. A date for the launch will be set, when ethical approval has been granted by the Ministry of Health and Social services as well as the UCT Research Ethics Committee, the latter can be contacted should there be any ethical concerns (0027-21-4066338)

Yours sincerely,

Maja Brand