AN EDUCATIONAL INTERVENTION TO REDUCE PAIN AND IMPROVE PAIN RELATED OUTCOMES FOR MALAWIAN PEOPLE LIVING WITH HIV/AIDS AND THEIR FAMILY CARERS: A RANDOMISED CONTROLLED TRIAL

Kennedy Nkhoma MSc; BSc. R.N

Thesis submitted to the University of Nottingham for the degree of Doctor of Philosophy

September 2015

Abstract

Background: Many HIV/AIDS patients experience pain. This is often associated with advanced HIV/AIDS infection and side effects of treatment. In sub-Saharan Africa, pain management for people with HIV/AIDS is suboptimal. With survival extended as a direct consequence of improved access to antiretroviral therapy, the prevalence of HIV/AIDS related pain is increasing. As most care is provided at home, the management of pain requires patient and family involvement. Pain education is an important aspect in the management of pain in HIV/AIDS patients.

Aim: The aim of this study was to evaluate the effects of a pain educational intervention on pain severity and pain related outcomes among patients with HIV/AIDS and their family carers.

Methods:

Two systematic reviews were conducted: (1) to examine the evidence base of the effectiveness of educational interventions delivered to people living with HIV/AIDS on pain severity, pain interference, quality of life, knowledge of pain management, and (2)

To examine the evidence base of the effectiveness of educational interventions delivered to their family carers on knowledge of pain management, quality of life and carer motivation.

A randomised controlled trial was conducted at the HIV and palliative care clinics of two public hospitals in Malawi. To be eligible, patient participants had a diagnosis of HIV/AIDS (stage III or IV). Carer participants were individuals most involved in the patient's unpaid care. Eligible participants were randomised to either: (1) a 30-minute face–to-face educational intervention covering pain assessment and management, augmented by a leaflet and follow-up telephone call at two weeks; or (2) usual care. Those allocated to the usual care group receive the educational intervention after follow-up assessments had been conducted (wait-list control group). The primary outcome was average pain severity measured by the Brief Pain Inventory. Secondary outcomes were pain interference, patient knowledge of pain

management, patient quality of life. Carer outcomes were; carer knowledge of pain management, caregiver motivation and carer quality of life. Follow-up assessments were conducted eight weeks after randomisation by nurses' blind to allocation.

Results:

Systematic review

Eight published randomised controlled trials of educational interventions among patients with HIV/AIDS were identified. Only one study examined the effect on pain severity but the results were not statistically significant. Three studies reported positive effects in improving severity and frequency of symptoms, three reported improvement in quality of life and two studies found improvement in knowledge. Seven published studies of family carers of HIV/AIDS patients were identified. Only three of which were randomised controlled trials. Five of these reported that educational interventions were effective in reducing psychosocial outcomes. Two studies reported that the interventions improved knowledge outcomes among family carers of HIV/AIDS patients.

Trial

Of the 182 patients/carers dyads randomised; 167 patients and 157 carers completed the trial. At follow-up, patients in the intervention group experienced a greater decrease in average pain severity score 21.25 (mean difference 21.25, 95% confidence interval 16.7 to 25.8; P <0.001). Patients in the intervention group reported, less pain interference (mean difference 24.5, 95% confidence interval 19.61 to 29.38; P<0.001), had improved knowledge of pain management (mean difference 20.39, 95% confidence interval 17.51 to 23.27; P<0.001), and a better quality of life (mean difference 28.76, 95% confidence interval 24.62 to 32.91; P<0.001). At follow-up carers in the intervention group had improved knowledge (mean difference 20.32, 95% confidence interval 17.37 to 23.28; P<0.001), greater motivation (mean difference 7.64, 95% confidence interval 5.15 to 10.13; P<0.001) and better quality of life (mean difference 34.16, 95% confidence interval 30.15 to 38.17; P<0.001).

Conclusion:

Current evidence of educational interventions among HIV/AIDS and family carers on pain severity is inconclusive and based on a relatively small number of studies, many of which have methodological problems.

A relatively simple form of pain education is effective in reducing pain and improving outcomes for patients with HIV/AIDS and their carers. Greater attention needs to be given to incorporating this into the routine care of people with HIV/AIDS in sub-Saharan Africa.

Trial registration: Current Controlled Trials ISRCTN72861423

List of outputs

Nkhoma K, Seymour J, Arthur A. 2015. An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: a randomised controlled trial. In press doi:10.1016/j.jpainsymman.2015.01.011. (Appendix 15).

Nkhoma, K., Seymour, J. & Arthur, A. 2013. An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: study protocol for a randomised controlled trial. *Trials,* 14**,** 216. (Appendix 15).

Nkhoma, K. 2014. An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: a randomised controlled trial *Lawrence S. Bloomberg Faculty of Nursing Emerging Scholars Forum October 20-21, 2014 Toronto, Canada*.

Acknowledgements

I give thanks to heavenly father for the protection and care throughout my PhD journey; I have had spiritual challenges, but my God has always been there.

I would like to thank my supervisors Professor Antony Arthur and Professor Jane Seymour for their constructive criticism throughout the PhD journey. I had no idea how to go about designing the study, but through their support and guidance I was able to conduct a trial, analyse data, publish some work, and attract funding for both short cources and conferences. I have learned a lot from them.

I would like to thank all the patients and family carers who were involved in designing the information leaflet, including all health care workers who were involved in designing the leaftlet.

Special thanks should go to all patients and family carers who took part in the study, their response and enthusiasm add a lot of strength to this study. They made the process of recruitment very interesting.

Many thanks to Amin and Oscar for conducting follow-up outcomes. All staff members at Ekwendeni and Mzuzu central hospital deserve a mention as well for their support in recruitment of patients and any form of support rendered to me during the field work.

I would also like to acknowledge the financial support provided by the University of Nottingham, School of Health Sciences (tuition fees) and the Malawi Government for my upkeep allowances without which it would have been impossible to undertake this research. You made my PhD journey a bit easier because I did not have to worry about finances.

I wish to thank Esther my lovely wife for her love, motivation and support during the PhD journey including all my family members; my parents, brothers and sisters for their spiritual support and guidance including prayers.

Finally all my friends in B33 (PhD office) for moral support, academic support including social support, and all my friends in different parts of the world.

TABLE OF CONTENTS

List of tables

List of figures

List of Abbreviations

AIDS: Acquired Immune Deficiency Syndrome

APCA: African Palliative Care Association

ART: Anti-retroviral Therapy

BPI: Brief Pain Inventory

CDC: Centre for Disease Control

CHAM: Christian Health Association of Malawi

DFID: Department for International Development

FPQ: Family Pain Questionnaire

GDP: Gross Domestic Product

HAART: Highly Active Anti-retroviral Therapy

HIV: Human Immunodeficiency Virus

IMF: International Monetary Fund

PCP: Pneumocystis Carinii Pneumonia

PCRS: Picot Caregiver Rewards Scale

PLWHA: People Living with HIV

POS: Palliative Care Outcome Scale

PPQ: Patient Pain Questionnaire

QoL: Quality of life

RCT: Randomised Controlled Trial

SSA: Sub-Saharan Africa

TB: Tuberculosis

UNAIDS: United Nations Program of HIV and AIDS

WHO: World Health Organisation

CHAPTER ONE: INTRODUCTION AND OVERVIEW

This research study examines and reports the effects of an educational intervention consisting of an information leaflet, face-to-face verbal discussion and two-week follow-up phone call on pain management for people living with HIV/AIDS (PLWHA) and their family carers in Malawi. In the first section of this chapter I outline the aims and objectives of the study. In the following section I describe the significance of the study, conventions and terminology used in the thesis. In the last section of this chapter I outline the structure of the thesis.

1.1 Aim of the study

The study aimed to evaluate the effects of an educational intervention on pain severity and perception of pain among people living with HIV/AIDS (PLWHA) and their family carers in Malawi.

1.2 Objectives of the study

The study was conducted in order to test the following hypotheses:

- Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will report less severity of pain.
- Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will report less interference of pain in their daily activities.

- Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will have a greater knowledge of pain management.
- Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will have a better quality of life.
- Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have greater knowledge of pain management.
- Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have greater motivation to provide care.
- Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have a better quality of life.

1.3 Significance of the study

HIV/AIDS remains a disease of great public health importance particularly in sub-Saharan Africa, home to 69% of all people living with HIV/AIDS (WHO, 2013). In recent years as a result of improved access to HIV treatment and care, and since the publication and introduction of new treatment and guidelines for HIV/AIDS (WHO, 2013), there has been a dramatic reduction in death rate (UNAIDS, 2010) with people infected with HIV/AIDS living longer (Deeks et al., 2013). HIV/AIDS is now classified as a chronic illness (Deeks et al., 2013, Scandlyn, 2000).

HIV treatment is associated with side effects such as peripheral neuropathy (Peltzer et al., 2008, Heath et al., 2003) which has negative effects on the quality of life for people living with HIV/AIDS (Hughes et al., 2004, Hughes, 2004, Hudson et al., 2004, Brechtl et al., 2001). Due to staff shortage in Malawi hospitals and due to the chronic nature of the condition of HIV/AIDS, most care is provided at home by family members in a familiar setting (Ministry of Health, 2011b). This means that family members play a significant role in the management of HIV/AIDS including the management of pain.

Pain is a significant problem in HIV/AIDS patients (Newshan and Sherman, 1999, Newshan, 1997, Harding et al., 2010a). HIV treatment does not cure AIDS, but reduces viral load in the body and strengthens the immune system (WHO/UNAIDS/UNICEF, 2011). HIV treatment needs to be taken for life to prevent drug resistance. Malawi has made good progress in improving access to HIV treatment for patients, with more than 52% of the population having access to HIV treatment (Malawi Government, 2012a). This has helped to reduce mortality among HIV/AIDS patients (UNAIDS, 2013), but treatment related pain remains an issue.

Systematic review of pain education among patients with HIV/AIDS reported conflicting results. One reported that HIV/AIDS pain education helps to improve the patient knowledge of pain management (Goujard et al., 2003), reduces symptom severity in men with HIV/AIDS (Gifford et al., 1998) and another trial found no evidence in women with HIV/AIDS (Webel, 2010). Another trial reported that quality of life outcomes were worse in the intervention group (Wu et al., 2006). A trial of a pain symptom management manual for HIV/AIDS patients found symptom

frequency reduced in the intervention group (Wantland et al., 2008). Only one study assessed pain as an outcome (Gifford, et al, 1998) and found no evidence of a positive effect. These studies were conducted exclusively (Gifford et al., 1998, Wu et al., 2006, Webel, 2010) and predominantly (Wantland et al., 2008) in western countries where the social and cultural context differs to that of Malawi.

Systematic review of pain education intervention among family carers of HIV/AIDS patients reported that psychosocial and psycho-educational interventions are effective in reducing depression, anxiety, distress and knowledge outcomes. These studies (n=6) were conducted predominantly in western countries except one study (Boon et al, 2009) which was conducted in South Africa. The outcomes of interest in these studies were mainly psychosocial with no study focussing spefically on education outcomes. Only one study (Pakenham, 2002) randomised both patients and family carers, however the sample size was too small (n=36). The educational materials tested such as DVDs, videos, manuals, are not accessible to most people in Malawi.

A pain education intervention, drawing on-adult learning theory was designed for both HIV/AIDS patients and family carers based on the inconclusive results from the systematic reviews. The pain education intervention study recruited patient and carer dyads. The intervention included a verbal face-to-face discussion, and a leaflet-based education entitled "All about your pain" and a phone call reminder after two weeks following the delivery of the intervention. A randomised controlled trial was conducted at two public hospitals in the northern part of Malawi to investigate the effects of the intervention on health outcomes of patients

and family carers. The primary outcome of this trial was average pain severity as reported by patients. Other patient outcomes of interest for this trial were the effect of the pain education intervention on patient pain interference, patient knowledge of pain management and patient quality of life. Carer outcomes for the trial were carer knowledge of pain management, care motivation in provision of care and carer quality of life.

1.4 Conventions and terminology used in the thesis

In this section I will describe and explain the meaning of the terms and concepts I use in the thesis. This is to enlighten the reader because some of these concepts may have a different meaning elsewhere.

The term 'Antiretroviral therapy' refers to drugs that stop viral replication so that the weakened immune system can recover in people infected with HIV/AIDS. These are drugs given to the people living with HIV/AIDS throughout their life span. The drugs are not a cure but reduce multiplication of HIV and viral load, and strengthens the immune system thereby preventing the development of AIDS. These drugs are normally given to people with a low CD4 count (<350 cells/mm3) or with advanced HIV/AIDS infection (clinical stages III and IV). The term 'highly active antiretroviral therapy' refers to a combination of two or more antiretroviral therapy. Previously there was only one antiretroviral therapy (monotherapy) known as Zidovudine, which became ineffective because of developed resistance. New antiretroviral drugs were developed that contains a combination of two or more drugs in order to maximally suppress the HIV virus and stop the progression of HIV disease or AIDS.

The term ‘opportunistic infection’ refers to diseases or infections that frequently attack the patient as a result of HIV infection. People living with HIV/AIDS can live with HIV for many years without feeling sick, but when the viral load increases, the HIV damages the body’s immune system. A person with a weakened immune system due to HIV will begin to develop opportunistic infections specific to people living with HIV/AIDS such as severe bacterial infections, skin rash, Kaposi’s sarcoma. The severity of these opportunistic infections is associated with the further weakening and destruction of the immune system.

The term ‘family carer’ refers to a primary care provider for people living with HIV/AIDS. These are typically family members, relatives, and friends, as well as neighbours who are directly and mostly involved in the provision of care to chronically or terminally ill persons with HIV/AIDS.

The term ‘home-based care’ refers to care provided to people living with chronic illnesses such HIV/AIDS, Cancer, and Tuberculosis in their own homes. The care may be provided by a family carer or health care staff members.

The word ‘I’ is used to enlighten the reader that I was responsible for implementing an action or activity in conducting the study. This has helped to avoid writing in the third person which would have possibly distanced me from the work I did.

1.5 structure of the thesis

The thesis has eight chapters. Chapter one introduces the study and provides the reader with a justification for conducting the randomised controlled trial and includes an overview of the thesis. Chapter two looks at the contextual background of HIV/AIDS. This chapter describes the epidemiology of HIV/AIDS globally, in the sub-Saharan region and Malawi. This chapter includes an explanation of the health care delivery system in Malawi and the challenges the country faces in providing care to people living with HIV/AIDS. Palliative care provision to people living with HIV/AIDS, an outline of the HIV/AIDS treatment for people living with HIV/AIDS and the clinic journey they travel is also outlined in this chapter. Chapters three, four and five contains a review of the literature about HIV/AIDS and pain in HIV/AIDS. Chapter three reviews literature about the prevalence of pain in HIV/AIDS, the significance of pain in HIV/AIDS, and the needs of patients and family carers of people living with HIV/AIDS. Care by family carers to people living with HIV/AIDS is outlined in this chapter. Chapter four reviews evidence from randomised controlled trials on the effects of educational interventions on pain management for people living with HIV/AIDS. This chapter contains a critical review and appraisal of the evidence reported from trials using a two or three group comparison design. Chapter five reviews evidence from randomised controlled trials on the effects of psychosocial and psycho-educational interventions on pain management for family carers of people living with HIV/AIDS. In this chapter I critically review and appraise studies conducted both in western countries and sub-Saharan Africa.

Chapter six contains the methodology and methods of the study. The rationale for the study design is discussed. Participant's recruitment, baseline assessments, the process of randomisation, the development, delivery and implementation of the pain education intervention, and follow-up assessments are discussed in this chapter. In the last section of this chapter I will discuss ethical considerations made in relation to the design and implementation of the pain education intervention.

Chapter seven reports the results of the randomised controlled trial. The recruitment and participants flow for the trial, baseline characteristics of study participants of the two parallel groups, uptake and adherence of the interventions, the differences observed between the two groups in terms of primary and secondary outcomes.

Chapter eight contains the strengths and limitations of the trial. The results are compared with other studies conducted elsewhere in HIV/AIDS field and other similar chronic conditions. Finally in this chapter I discuss the implications of the pain education intervention study for practice, policy and education for HIV/AIDS care, recommendations are provided for future research.

CHAPTER TWO: CONTEXTUAL INTRODUCTION AND BACKGROUND

This section contains the significance of HIV/AIDS globally, in African and more specifically in the sub-Saharan region of Africa, and in Malawi, including the social, economic, and psychological impacts of HIV/AIDS on society. The clinical staging of HIV/AIDS is explained according to the World Health Organisation (WHO) and Centre for Disease Control (CDC) eligibility criteria for HIV treatment. The next section describes the health care delivery system in Malawi, and the challenges experienced in the health sector. The last section describes the role of palliative care for people living with HIV/AIDS, antiretroviral therapy, the clinic journey of people living with HIV/AIDS and health education provision among HIV/AIDS patients and their family carers in Malawi.

2.1 Background

2.1.1 HIV/AIDS

Acquired immunodeficiency syndrome (AIDS) is a surveillance definition based on signs, symptoms, infections, and cancers associated with the deficiency of the immune system that stems from infection with HIV (Kemp et al., 2003). AIDS is a collection of signs and symptoms associated with life-threatening immune deficiency caused by Human Immune Deficiency Virus (HIV), a human retrovirus (Kemp et al., 2003). HIV/AIDS has existed for more than three decades, the first AIDS cases were reported in 1981 in the USA. HIV/AIDS remains a disease of public health importance and one of the highest causes of mortality and morbidity in the modern world

(WHO, 2011b). AIDS is not simply a medical problem but due to its associated morbidity and mortality, every aspect of an individual's life is vulnerable (Morrison, 1993). HIV is a virus (of the type called retrovirus) that infects cells of the human immune system (mainly CD4 T-cells and macrophages—key components of the cellular immune system), and destroys or impairs their function. HIV mostly is asymptomatic; as such it is not possible to know whether or not one has HIV without a blood test to confirm the status. Infection with this virus results in the progressive deterioration of the immune system, leading to immune deficiency (Kemp et al., 2003, Kaplan et al., 2009).

The immune system is considered deficient when it can no longer fulfil its role of fighting off infections and diseases. Immune deficient people are more susceptible to a wide range of infections, most of which are otherwise rare among people with a strong immune system (Cairns et al., 2006). Infections associated with severe immunodeficiency are known as 'opportunistic infections', because they take advantage of a weakened immune system (Kaplan et al., 2000). At this point, the individual presents with signs and symptoms and is said to have AIDS (WHO, 2007).

HIV is staged on the basis of certain signs, symptoms, infections, and cancers grouped by the World Health Organization (WHO). There are four stages of HIV/AIDS infection:

- Clinical stage 1 - asymptomatic or generalized swelling of the lymph nodes.
- Clinical stage 2 - includes minor weight loss, development of shingles and recurrent upper respiratory tract infections.

- Clinical stage 3 - includes unexplained chronic diarrhoea, unexplained persistent fever, oral candidiasis, severe bacterial infections like pneumonia, weight loss more than 10% unintentionally, pulmonary tuberculosis and acute necrotizing inflammation in the mouth.

- Clinical stage 4- where there is HIV wasting syndrome with extra pulmonary tuberculosis, Oesophageal candidiasis, Kaposi's Sarcoma or Pneumocystis carinii pneumonia (WHO, 2007, WHO, 2005).

The Centre for Disease Control and Prevention (CDC) and WHO have developed critical tools for monitoring HIV epidemic and also for use by clinicians to provide appropriate care to patients. CDC uses the CD4 count system. Patients with low CD4 count (<350 cells or CD4 percentage <14%) should be put on HIV medication known as antiretroviral therapy (ART) or Highly Active Antiretroviral therapy (HAART) (Centre for Disease Control, 1993, WHO, 2007), although according to new WHO guidelines (WHO, 2013) anyone who has tested HIV positive needs to start HIV treatment regardless of their CD4 count.

The WHO system is applicable in resource poor countries like Malawi where CD4 count equipment is not available in most health facilities, and even where available they are not accessible to many patients, since facilities may not have the necessary reagents to conduct the tests.

2.1.2 The Global epidemiology of HIV/AIDS

In this section I explain the HIV/AIDS situation in the world.

According to global estimates from (UNAIDS, 2013, WHO, 2013) around 35.3 million people (32.1 million adults and 3.3 million children under 15 years of age) were living with HIV at the end of 2012. More than half (17.7 million) of the infected adults were women. The year 2012 also saw 1.6 million deaths from AIDS, a reduction from 2.3 million deaths in 2005. There were 2.3 million newly infected globally, showing a 33% decline in number of new infections from 3.4 million in 2001. This has been due to expansion in prevention efforts like health education and treatment. In 2010 alone 1.4 million people were started on HIV medication globally, increasing the number of people receiving treatment by 27% in a single year. This expansion of treatment led to a 19% decline in deaths among PLWHA between 2004 and 2009 (UNAIDS, 2010).

In summary there were globally, 35.3 million PLWHA at the end of 2012 compared to 26.2 million PLWHA in 1999, a 28% increase in the number of PLWHA, however the death rate and infection rate decreased due to the significant scale-up of treatment with HIV medication (UNAIDS, 2010, WHO, 2011b, WHO, 2013).

Table 1 Global HIV/AIDS Estimates as of end 2012 (WHO 2011b, WHO, 2013)

Item	**Estimate**
People living with HIV	35.3 million
Adults with HIV	32.1 million
Children with HIV	3.3 million
Newly infected	2.3 million
Deaths	1.6 million

2.1.3 The epidemiology of HIV/AIDS in Sub-Saharan Africa

In this section I highlight the HIV/AIDS situation in the sub-Saharan region. I also highlight the most affected countries in the sub-Saharan region including Malawi.

The overwhelming majority of people with HIV, some 95% of the global total, live in resource poor countries (UNAIDS, 2010). Sub-Saharan Africa (SSA) is by far the worst-affected region. It has 10% of the world population, but is home to 69% of all people living with HIV. AIDS killed about 1.3 million people in 2010 in this region. Antiretroviral therapy (ART) dramatically extends survival, allowing many years of healthy life, but remains unavailable in many parts of the region (UNAIDS, 2010)**.** However in SSA at the end of 2010, the number of people treated with antiretroviral drugs increased from 37% in 2009 (Callaghan et al., 2010) to 49% of the population eligible for treatment (WHO/UNAIDS/UNICEF, 2011).

The worst affected countries in SSA are: South Africa, Zimbabwe, Lesotho, Malawi, Zambia, Namibia, Swaziland, Angola, Mozambique, and Botswana. In these countries, by the end of 2009, there were 11.3 million PLWHA, which comprises 34% of the global total, 31% of new infections and 34% of AIDS related deaths (UNAIDS, 2010). However in these countries there has been a decrease in AIDS related deaths by 18% (UNAIDS, 2010, WHO, 2011b). This has implications for the practice and delivery of home based care and palliative care for PLWHA, since there are some who have no access to treatment, while those who are accessing treatment need better quality care (including supportive care) as they are living longer.

Table 2 HIV/AIDS in SSA and Malawi as of end 2012 (WHO, 2011b, WHO, 2013)

Item	Estimate	Proportion of global HIV cases
SSA		
People living with HIV Newly infected Deaths	25 million 1.6 million 1.2 million	69%
Malawi		
People living with HIV New infections Deaths	910,000 250/day 51,000	11%

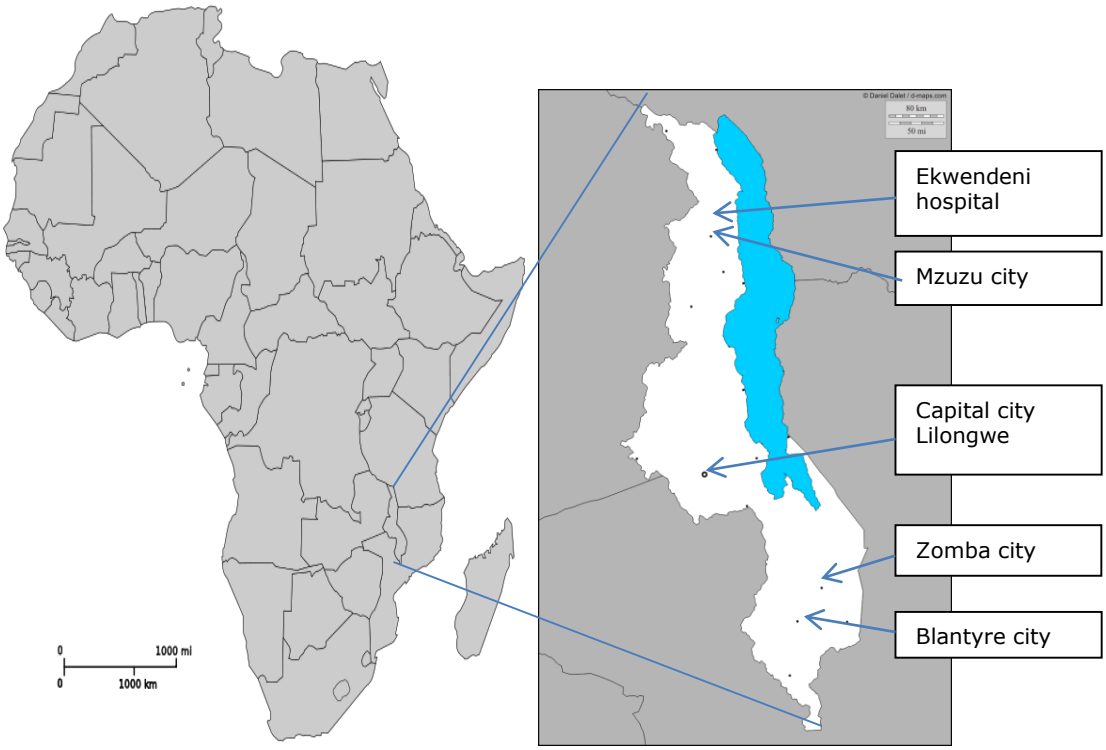
2.1.4 The Burden of HIV/AIDS in Malawi

This section contains a highlight of the situation of HIV/AIDS in Malawi where this study was conducted. The burden of HIV/AIDS to the country, family and individual including the social and economic effects is explained in this section.

Malawi is one of the 47 countries in the sub-Saharan region of southern Africa (see figure 1). There is a high prevalence of HIV/AIDS with an estimated 910,000 people living with the disease at the end of year 2012. This represents 11 % of the population of those aged between 15 and 49 years (WHO, 2013). The year also saw 51,000 deaths, with 650,000 children orphaned due to AIDS deaths (UNAIDS, 2010, WHO, 2011b).

The observed and adjusted HIV prevalence among women and men aged 15-49 years were 11.8% and 12.7% respectively (UNAIDS, 2010). Approximately 250 new people are infected each day, and at least 70% of Malawi's hospital beds are occupied by HIV/AIDS patients (Kumwenda, 2005), making Malawi the 10th -worst country affected with HIV/AIDS worldwide (Central Intelligence Agency, 2013). Life expectancy at birth is

Figure 1: Map of Africa in relation to Malawi



58 years for males and 62 years for females. In comparison with UK, males have a life expectancy of 78 years while females have 83 years. Malawi has a low life expectancy, its ranked on 194th position worldwide (Central Intelligence Agency, 2013).

The high prevalence of HIV/AIDS is a drain on the labour force and government expenditures, with an estimated 5.8% of the farm labour force

dying of the disease. HIV/AIDS was expected to lower the country's gross domestic product by at least 10% by 2010 (WHO, 2006a). The government spends over U$120,000 each year on funerals for civil servants who die of the disease (Matewele, 2004, United Nations Development Programme, 2002).

Substantial progress has been made in the provision of ART/HAART. By the end of 2011, an estimated 325,000 people had been started on ART/HAART compared to 13,200 in 2004 (UNAIDS, 2012). However due to inequitable health system access to ART/HAART still remains a problem for others who need it (Makombe et al., 2008a, Ministry of Health, 2004, McCoy, 2003, Sabin, 2002). One mechanism Malawi has put in place to deal with the challenge of accessing HIV medication is by involving nurses to prescribe and administer these drugs. In addition the country has trained health assistants to provide HIV counselling services to patients rather than waiting for nurse counsellors, and this has resulted in some patients starting HIV medication within three weeks rather than waiting for three months after HIV diagnosis (WHO, 2011b).

There is a significant shortage of human resource in Malawi. The nurse and doctor to patient ratio is low; there are only 38 nurses and 2 physicians - per 100,000 populations (Ministry of Health, 2008a). Health professionals in the districts face high workloads: as many as 150 to 200 consultations a day. These shortages make it nearly impossible to provide good-quality healthcare and improve HIV services. It has recently been reported that Malawi has only 25% of the required number of nurses (Mphande, 2014). Other reasons why staff numbers are so low is sickness and death among health care workers that is often HIV-related, migration of doctors and

nurses to private sectors and overseas (Lawson et al., 2008). In 2010, the vacancy rate for nurses was 74% (Central Intelligence Agency, 2011). The National Organisation of Nurses and Midwives of Malawi, estimates that every month four nurses die due to HIV related conditions (The Daily Times, 2008). Morbidity and mortality is high among health workers (Swartz and Dick, 2002). In Malawi it is estimated that one in four hospital workers were lost to TB and AIDS over 10 years (Harries et al., 2001).

In an effort to address some of these issues, the government of Malawi in conjunction with its development partners such as DFID implemented a 5-pronged 6-year Emergency Human Resources Plan from 2005- 2010 which included:

- A 52% salary top up to 11 cadres of health professionals, and provision of incentives to health workers practising in rural areas.
- Expanding domestic capacity training for nurses and doctors.
- Use of international volunteer doctors and nurse tutors to cover up in the hospitals and training institutions.
- Provision of international technical assistance.
- Strengthening monitoring and evaluation capacity (WHO, 2011a, Manafa et al., 2009).

This resulted in a 50% increase in healthcare work-force and enrolment in training institutions (O'Neil et al., 2010). The challenge now is to maintain progress (WHO, 2011a).

2.2 Health care services in Malawi

Malawi is a developing landlocked country in Southern Africa occupying over 118,484 square km (Ministry of Health, 2005), with an estimated population of 15,879,252 (Central Intelligence Agency, 2011). It borders Tanzania in the north and north east (475 km), Zambia in the west and north west (837 km) and Mozambique in the east and south west (1569 km). It was under the British protectorate from 1891, until 1964 when it became independent. In terms of development in all aspects like economy, health care services, infrastructure Malawi is ranked number 165 of 223 countries worldwide, and it is number 33rd of 47 countries in Africa,(United Nations Development Programme, 2002). Malawi is one of the poorest nations in the world with 65.3% of the population living below the poverty line (National Statistical Office, 2003, Ministry of Health, 2005).

Malawi has four main cities: Mzuzu city in the northern region; Lilongwe (the nation's capital city) in the central region; Zomba and Blantyre in the southern region. Blantyre is the biggest and the most commercial city of Malawi (Figure 2).

Malawi is divided into three regions (northern, central and southern) and it has 28 districts in total. There are 6 districts in the north, 9 districts in the centre and 13 districts in the south. Each district has a hospital named after the name of that district. Within each district, there are administrative sub-divisions known as Traditional Authorities which are presided over by the chiefs. The smallest administrative unit is the village. There are four central hospitals in Malawi, two in the south, namely Zomba central hospital in Zomba city and Queen Elizabeth central hospital in Blantyre city.

There is also one in the centre (Kamuzu central hospital in Lilongwe city) and one in the north (Mzuzu central hospital in Mzuzu city).

2.2.1 Health care delivery systems in Malawi

Malawi's health policy aims at uplifting the health standards of the citizenry through a sound health care delivery system (Ministry of Health, 1995).

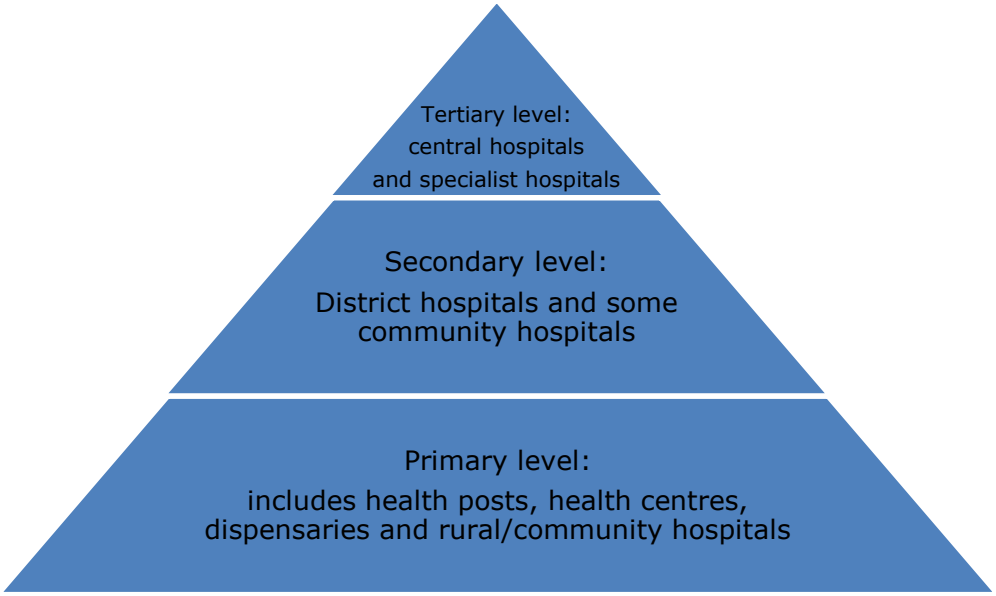
The delivery of health care services is structured into three main levels (Figure1) primary (health posts, health centres, dispensaries, rural/community hospitals), secondary (district hospitals and some community hospitals), and tertiary (central hospitals and specialised hospitals) (Global AIDS Programme, 2006). The Ministry of Health provides 60% of health services, followed by the Christian Health Association of Malawi (CHAM) (35%). Local authorities, large companies and private clinics provide the rest of health care services (Ministry of Health, 1999). Unlike CHAM, which charges user fees for its services, the bulk of health services provided by the government are free of charge (Global AIDS Programme, 2006).

As most health facilities in rural areas are under staffed in comparison with urban areas the poor are often disadvantaged in accessing essential services (Ministry of Health, 1995, Kemp et al., 2003, Gwatkin et al., 2004). The provision of HIV medication is not available in most parts of the rural areas as such patients and their family members have to travel long distances, often more than 20km, in order to receive medical attention. Some community hospitals in rural areas do provide HIV medication, but

they do not have CD_4 count facilities, thereby relying on WHO clinical stages.

Health care delivered by church institutions are implemented through Christian Health Association of Malawi (CHAM). This was established in 1966 to advise the churches on health issues, it also complements government efforts in providing health care services to local communities. CHAM has 171 member health facilities (including 10 teaching hospitals, 20 major hospitals, 30 community hospitals and health centres with or without maternity facilities). The facilities employ around 7000 employees country-wide[a].

Figure 2: Levels in the health system in Malawi



2.3 Socio-economic impact of HIV/AIDS

[a] http://www.actalliance.org/about/actmembers/christian-health-association-of-malawi-

2.3 Socio-economic impact of HIV/AIDS

Taking care of a person sick with AIDS is not only an emotional strain for household members, but also a major strain on household resources (Chimwaza and Watkins, 2004, Kipp et al., 2007b). Loss of income, additional care-related expenses, the reduced ability of caregivers to work, and mounting medical fees push affected households deeper into poverty (Casale and Whiteside, 2006, Greener et al., 2000). It is estimated that, on average, HIV-related care can absorb one-third of a household's monthly income (Salinas and Haacker, 2006, Casale and Whiteside, 2006).

The financial burden of death can also be considerable, with some families in Malawi easily spending seven times their total household monthly income on a funeral (Rabson et al., 2007). Funerals are expensive because sometimes it takes three days for the ceremony to be conducted and in Malawi mourners will gather at the house of the bereaved/deceased, meaning that food and shelter need to be provided by the bereaved family (Mtika, 1998). HIV/AIDS has also increased the workload of hospitals where more than 70% of bed occupancy is due to AIDS related illnesses (Government of Malawi, 2009). HIV/AIDS results in deaths of a productive demographic group like teachers, health care workers, and other civil servants (Malawi Institute of Management, 2008).

The HIV/AIDS virus has disproportionately infected the economically active age group (15-49 years) and this is the group that works hard in the field. The long period of HIV/AIDS illness therefore reduces labour production both in agriculture and companies (Haacker, 2004). This negatively affects the country's economy (Mtika, 1998, Hemrich and Schneider, 1997). The

AIDS epidemic adds to food insecurity in many areas, as agricultural work is neglected or abandoned due to household illness. In Malawi where food shortages have had a devastating effect, it has been recognised that HIV and AIDS have diminished the country's agricultural output (UNAIDS, 2010, Bollinger et al., 2000). There is a loss of agricultural productivity, it has been recognised that HIV/AIDS is diminishing the country's agricultural output. It was calculated in 2006 that by 2020, Malawi's agricultural workforce will be 14% smaller than it would have been without HIV and AIDS (Government of Malawi, 2009, WHO, 2006a). This is a big threat and challenge to the economy since Malawi relies on agriculture for its economic growth and labour for agricultural production.

Apart from the financial burden, providing home-based care and palliative care can impose demands on the physical, mental and general health of carers, usually family and friends of the sick person. Such risks are amplified if carers are untrained or unsupported by a home-based care organisation (Lindsey et al., 2003, Kipp et al., 2007a). Despite looking after the sick, in many households HIV/AIDS children are orphaned at a young age. The United Nations define an orphan as a child 18 years or less who has lost one or both parents (UNAIDS, 2006). These children are often looked after by their grandparents who may not have adequate income to support them for their education, food, shelter and other basic needs (Jones, 1997, Jones, 2006, Norse, 1992). Worldwide it is estimated that 16 million children under the age of 18 have lost one or both parents due to AIDS, and around 14.8 million of these live in SSA (UNAIDS, 2010).

In Malawi, by the end of 2009, it was estimated that over half a million of children are orphans due to AIDS (UNAIDS, 2010). An important aspect of

the government's strategy has been to promote and support community based programmes. In both rural and urban areas across Malawi, communities are developing a variety of ways to cope with the growing crisis of AIDS orphans. In many villages orphan committees have been established to monitor the local situation and to take collective action to assist those in need (Rowan and Kabwira, 2009, Phiri and Webb, 2002). However my personal observation is that funding is a problem to sustain such projects and previous literature (Mutume, 2001) reports that success is dependent on volunteers, a strategy that threatens its sustainability.

The Malawi Government in 2005 launched The National Plan for Orphans and other Vulnerable Children as a way to further its commitment to AIDS orphans, with the aim to increase access to essential services and to help families and communities provide support for such children (Government of Malawi, 2005), but implementation has suffered extensively due to delays (Sibale and Nthambi, 2008).

2.4 Antiretroviral therapy (ART) and Highly Active Antiretroviral therapy (HAART)

Although HIV/AIDS continues to be a problem worldwide, the availability of HIV medication through the reduction in prices and scaling up strategies for infected individuals in developing countries have made treatment accessible to some patients (Sacktor, 2002, WHO, 2011b, WHO, 2013). The first HIV medication to be introduced was Zidovudine, but developed resistance rendered it ineffective, this is what usually is known as antiretroviral therapy (ART). Therefore new HIV medications were

developed and put into clinical practice as a combination of Zidovudine and other drugs, this combination therapy is what is referred to as Highly Active Antiretroviral therapy (HAART). It combines three or more HIV medications to counteract the effects of HIV, hence also known as combination therapy. HAART slows the spread of HIV in the body, prevents illnesses and prolongs life. These drugs are administered to patients with advanced HIV infection (stages III and IV) or those with a CD_4 count of less than 350 cells mm^3 (WHO, 2007, WHO, 2010).

With the introduction of ART/HAART, HIV/AIDS patients are living longer (Deeks et al., 2013, Scandlyn, 2000), unlike in the early 1980s when the AIDS epidemic began, PLWHA were not likely to live more than a few years. Currently available drugs do not cure HIV infection but they do prevent the development of AIDS. They can suppress HIV from multiplying in the body and this stops the virus from damaging the immune system, but these drugs cannot eliminate HIV from the body (Botes, 2003, Hicks et al., 2003). Hence, people with HIV need to take HIV medication for life (Paredes and Clotet, 2003).

Since 1996 the use of ART in combinations of three or more drugs in countries where they are widely accessible has dramatically improved the quality of life for people with HIV and prevented them from premature death (Makombe et al., 2006, Makombe et al., 2008a). In Malawi free ART started in 2004 and this has brought significant change to PLWHA (Harries et al., 2006, Makwiza et al., 2009).

One of the consequence of increased access to HIV medication is the issue of treatment side effects (Subbaraman et al., 2007). HAART dramatically

prolongs the lives of PLWHA by reducing viral load, and strengthening the immune system, however there are serious side effects such as abdominal pain, peripheral neuropathy, nausea and vomiting. These require effective management (Collins and Harding, 2007). Neuropathic pain occurs due to HIV infection itself as well as due to the side effect of HIV medication (Wadley et al., 2011, Wadley et al., 2010), but mainly it occurs due to the effects of Stavudine, one of the components of combined therapy (Wadley et al., 2011).

WHO recommends that Stavudine should be phased out, but resource poor countries have not been able to find an alternative due to the cost alternative components (Long et al., 2010). Therefore as long as patients infected with HIV take this medication we should expect them to experience neuropathic pain. It has been reported that 57% of those treated with HIV medication had neuropathic pain and 77% of those reported that the pain was moderate to severe in a study by (Wadley et al., 2011).

In the year 2012, around 9.7 million people living with HIV had access to antiretroviral therapy in low- and middle-income countries. This represents 61% of people eligible for treatment under the 2010 WHO guidelines (WHO/UNAIDS/UNICEF, 2011); and 34% of people eligible under the 2013 WHO guidelines (UNAIDS, 2013, WHO, 2013).

In recent years, Malawi has made success in improving the country's HIV treatment response by implementing WHO guidelines (Malawi Government, 2012a). Some patients have been started on more effective drugs with less side effects, patients have started treatment earlier and pregnant women

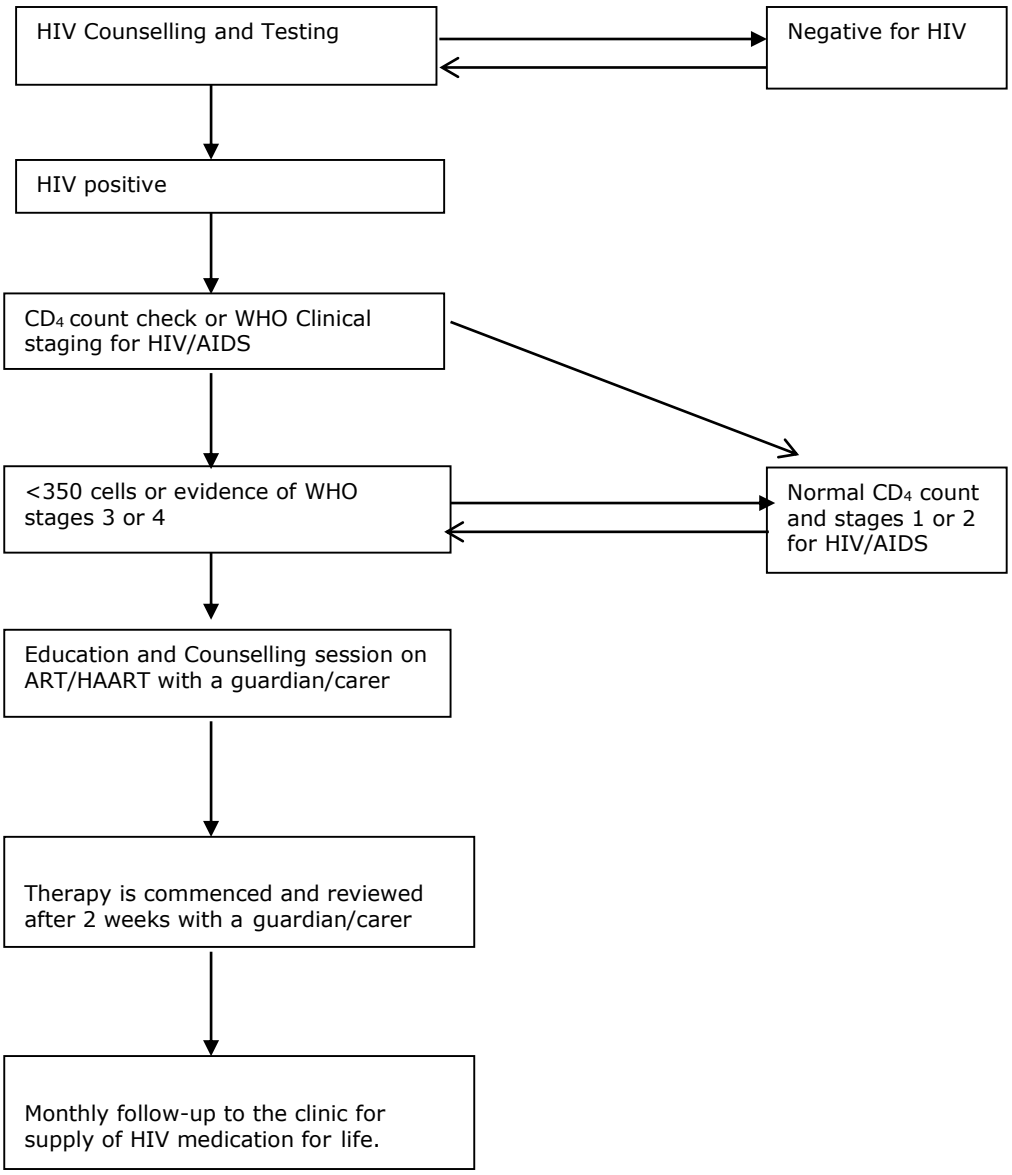
who are HIV positive are placed on treatment regardless of the CD4 count or WHO clinical stages (Malawi Government, 2012a).

2.4.1 ART/HAART provision in Malawi

In Malawi the patient is put on ART/HAART after undergoing a number of clinical investigations. First the patient goes for HIV counselling and testing and after being found positive s/he is tested for CD_4 count, and when CD_4 count is <350 cells/mm3 , the patient is placed on ART/HAART. When the CDC system is not available, WHO clinical staging is used (Ministry of Health, 2006, WHO, 2010, National AIDS Commission, 2003).

All the patients in Malawi who are to start ART/HAART are requested to attend with a carer who together with the patient receives health education and information on the importance of treatment compliance and the need to take the drugs every day for life (Ministry of Health, 2006, Makombe et al., 2008b). The carer in most cases is a close relation of the patient who stays with the patient. After a class session about ART/HAART implications and importance of treatment compliance the patient can start treatment. Usually the patient is seen after 2 weeks following therapy initiation and then routinely every month for clinical assessment and drug dispensing or drug refill (Ministry of Health, 2006). Figure 3 is a summary of the ART/HAART clinic journey which patients and their carers have to travel through.

Figure 3 The ART/HAART Clinic Journey



2.5 Health education among HIV/AIDS patients and family carers in Malawi

In Malawi all people living with HIV/AIDS receive health education prior to initiation of ART/HAART. Health education is provided by staff nurses, clinical officers who have received training about HIV/AIDS treatment and care provision to people living with HIV/AIDS. All the patients attend the health education session with their family carers (no patient is allowed to attend the session without a family carer and therefore cannot start HIV treatment). The education session is provided during first registration to the HIV clinic and focuses on drug adherence in order to prevent development of resistance strains of HIV. Health education emphasises on basic facts about HIV/AIDS, the drugs used to treat HIV/AIDS and how the drugs work, nutrition in HIV/AIDS, positive living with HIV/AIDS, prevention of spread of infection to others and side effects of HIV treatment. Usually patients are told to come to the hospital if they experience severe side effects such as abdominal pains, jaundice and skin rash.

2.6 Palliative care for people living with HIV/AIDS

Palliative care is 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, psychosocial and spiritual (WHO, 2002).

Palliative care is concerned with the assessment and management of pain and other symptoms among patients and their families with life limiting illnesses including physical, emotional/psychological and spiritual pain (Ventafridda, 2006). Palliative care is necessary to provide social, emotional and spiritual support for both the patient and their family from the time of diagnosis (Sepulveda et al., 2002). A strong body of evidence has demonstrated that palliative care can relieve the suffering of patients and families with terminal disease (Smalbrugge et al., 2007, Merriman and Harding, 2010, Harding et al., 2005). Many patients present late when they already have advanced disease and may be suffering from opportunistic infections (Harding et al., 2005). About 10% of HIV/AIDS patients develop immune reconstitution inflammatory syndromes (IRIS), many other patients experience undesired side effects and drug toxicities (Matheny, 2001). HIV related cancers such as Kaposi's sarcoma persists in spite of HIV medication and these are often not treatable in resource poor countries (Matheny, 2001). Palliative care is important in order to achieve the best quality of life for both the patients and families (Harding et al., 2003), a very important aspect of quality of life is being free from pain (Smalbrugge et al., 2007).

Palliative care is necessary along with ART/HAART due to the distressing and complex symptoms experienced by the patients (Harding et al., 2006, Sherr et al., 2007). The cornerstone of palliative care is the relief of pain and other distressing symptoms-although palliative care cannot be said to be present if pain control is the only intervention available (Merriman and Harding, 2010), and hence the need for a holistic approach to palliative care. Dame Cicely Saunders recognised that other factors can influence

pain and she developed the concept total pain as a way of assessing and managing pain in chronic illnesses which looks at the physical, social, spiritual and psychological aspect of the human being (Watson et al., 2009). The pain education study uses a holistic approach into the assessment and management of pain among HIV/AIDS patients and their family carers. The components of the pain education intervention consisted of the biological (pharmacological) management of pain through adequate and effective use analgesia, psychological management of pain through provision of information, support and knowledge to minimise distress associated with poorly controlled pain and social management of pain by targeting the intervention at patient/carer dyad level (Nkhoma et al, 2013).

The pain education intervention is about both pain relief and palliative care. This is because relief of pain and suffering is a key component of palliative care. Palliative care requires a holistic approach such as provision of interventions to minimise discomfort and suffering, psychological support to reduce distress due to pain experience and social support to minimise social problems such as lack of available family support. Palliative care seeks to provide support to the family, as well as relieving pain and suffering. The pain education intervention attends to three fundamental aspects of palliative care: (1) the relief of pain and suffering, (2) the provision of help and support to the family and (3) the use a team approach (patient, family carer, health care professional in this instance) to improve patient care.

2.7 Chapter summary

HIV/AIDS is still a disease of public health importance particularly in the sub-Saharan region, however infection rates are stabilising, access to HIV treatment is improving, and people are living longer. HIV/AIDS has social, psychological and economic impacts in society, particularly in resource poor countries such as Malawi. HIV/AIDS has infected and affected the most productive section of the population (15-49 years) and hence loss of productivity in agriculture and low exports revenues from the fields. HIV/AIDS has become a chronic illness and therefore requires a palliative care approach in order to meet the physical, social, psychological and spiritual needs of patients and their families. Pain and other symptoms experienced by people living with HIV/AIDS are explored in the next chapter.

CHAPTER THREE: PAIN AND SYMPTOMS AMONG PEOPLE LIVING WITH HIV/AIDS

3.1 Introduction

In this chapter the significance of pain and its related symptoms in people living with HIV/AIDS is examined. The literature around the epidemiology of pain in HIV/AIDS and how pain affects quality of life is reviewed. An exploration of pain assessment and management in the clinical setting is provided. This chapter examines the experiences of family carers of people living with HIV/AIDS, their roles and the challenges they experience in providing home-based care to patients living with HIV/AIDS. The final section of the chapter explores literature on the needs of patients and their family carers.

3.2 Pain in people living with HIV/AIDS: defining pain

Pain is a significant problem for people living with HIV/AIDS (Harding et al., 2010a, Newshan, 1997, Newshan and Sherman, 1999). Advanced HIV infection and its treatment are associated with intense physical and psychological symptoms. These require focused assessment and management using locally available resources and interventions to ensure good quality of life for patients and their carers. Pain is defined as whatever the patient says it is and only exists when the patient says it does (Mc Caffery and Beebe, 1989). The International Association for the Study of Pain (IASP, 1996) defined pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or

described in terms of such damage. In this study I have adopted the IASP definition of pain but mindful that ultimately pain is a unique experience for individual patients and therefore the position of McCaffery and Beebe (1989) is also taken into account. This is because the outcomes in this study were all self-reported by the patients and this is in line with the former definition of pain. The theoretical framework for this study 'the biopsychosocial model' is in line with the latter definition of pain.

The two systematic reviews reported in chapters four and five: (1) pain educational interventions among HIV/AIDS patients, and (2) pain educational interventions among family carers of HIV/AIDS patients respectively are both inconclusive. The studies reviewed had methodological challenges and were poorly described. It is these inconclusive results from the two reviews that informed the decisions around the choice of study participants in the current trial (1) HIV/AIDS patients and (2) their family carers.

3.3 Epidemiology of pain in HIV/AIDS

In this section I highlight the significance and prevalence of pain among HIV/AIDS patients.

Pain is one of the most prevalent, frequent and debilitating symptoms in patients with HIV/AIDS (Cox and Rice, 2008, Breitbart et al., 1996, Norval, 2004, Rosenfeld et al., 1996) particularly in its later stages (Collins and Harding, 2007, Breitbart, 1996b, Breitbart et al., 1998). Between 30 and 90 percent of AIDS patients suffer from pain at some point in their illness (Solano et al., 2006, Karus et al., 2005, Breitbart et al., 1998).

Pain in HIV infection is experienced throughout the disease trajectory (Selwyn, 2005, Solano et al., 2006, Peltzer et al., 2008). Pain is mainly experienced in advance infection of HIV and it is estimated that 80% of people with advanced HIV infection experience severe pain (Solano et al., 2006), like cancer pain the severity of HIV pain increases as the disease progresses (Hewitt et al., 1997, Glare, 2001, Coughlan, 2003). One study of models, services and challenges of end of life care provision in 14 countries in sub-Saharan Africa reported that 98% of the services for HIV/AIDS patients are home-based and that 94% of the respondents reported that they experienced challenges to providing pain relief (Harding et al., 2003). It is suggested that most people in sub-Saharan Africa died from AIDS in pain in 2003 (Merriman and Harding, 2010).

In Malawi pain is the main symptom reported by HIV/AIDS patients (Tapsfield and Jane Bates, 2011). In another study HIV/AIDS patients had reduced quality of life compared to their counterparts without HIV and were in severe pain as the infection advanced (Fan et al., 2011). A recent systematic review reported that pain is present among 55 to 67 percent of PLWHA at all stages of the disease (Parker et al., 2014). People with HIV do experience pain in all parts of the body as the infection advances from HIV-related opportunistic infections and from HIV-related cancers such as Karposis sarcoma (Grant et al., 2011). Most pain experienced by people living with HIV/AIDS has an underlying treatable cause (Hewitt et al., 1997) such as treatable infections, and reversible medication effects (Marcus et al., 2000).

Types and levels of pain vary by individual and the respective stage of HIV infection. In the early stages of infection, around 30 percent of people with

a CD_4 count of >500 cells mm^3 experience mild pain (Rosenfeld et al., 1996, Breitbart et al., 1996, Larue et al., 1997). Lower CD_4 counts are associated with higher prevalence of pain (Richardson et al., 2009, Aouizerat et al., 2010, Dobalian et al., 2004). Higher prevalence and severity of pain is associated with advanced stages (III or IV) of HIV/AIDS infection (WHO, 2006b, Martin et al., 1999, Dobalian et al., 2004, Nair et al., 2009). However other studies have reported no difference in pain prevalence with stage of illness or CD_4 (Breitbart et al., 1996, Del Borgo et al., 2001, Wahab and Salami, 2011), similarly (Vogl et al., 1999, Wakeham et al., 2009, Wakeham et al., 2010) reported that high levels of symptoms were observed in all stages of HIV infection suggesting that WHO system and CD_4 count may not be the only system to predict prevalence of painful symptoms in HIV infection. Other studies have reported that there is no correlation between levels of CD_4 cells and measures of pain in HIV infected individuals (Van As et al., 2009, Peltzer and Phaswana-Mafuya, 2008, Rosen et al., 2008). In a multicentre observational study (Simms et al., 2013) HIV patients in all stages reported multidimensional problems at the initial HIV diagnosis. In a cross-sectional study it is reported that 66% of patients in the study reported pain: predominantly headache, nociceptive pain (68%) and neuropathic pain (32%), which significantly affected the quality of life of the patients. However this was a small pilot study so findings need to be treated with caution (Nair et al., 2009). Lower CD_4 counts are also associated with experiencing pain in a greater number of sites (Martin et al., 1999). HIV patients usually report multiple painful sites, most sites reported in literature are lower limbs, headache, abdominal pain, musculoskeletal and chest pain (Wahab and Salami, 2011, Peltzer and Phaswana-Mafuya, 2008, Makoae et al., 2005).

Because HIV is now a chronic illness, the pain experienced by people living with HIV/AIDS is also chronic. Studies report that peripheral neuropathy is the primary source of chronic pain in HIV which usually occurs due to treatment and HIV infection (Kamerman et al., 2012, Wadley et al., 2011).

3.4 Effects of HIV/AIDS pain on the patient

In this section, I highlight the effects of HIV/AIDS pain on psychological, emotional and social aspects of quality of life. I also highlight HIV/AIDS pain interference on daily life activities among HIV/AIDS patients.

The negative impact of pain on quality of life has been reported (Wahab and Salami, 2011, Sukati et al., 2005). Severe pain can reduce adherence to drugs and the quality of life of HIV/AIDS patients as reported by several authors (Holzemer et al., 2001, Hughes et al., 2004, Hughes, 2004, Brechtl et al., 2001, Hudson et al., 2004). Pain is the most frequent and main cause of psychological distress (Vogl et al., 1999, Marcus et al., 2000, Rosenfeld et al., 1996, Rotheram-Borus, 2000) depression and emotional distress (Rotheram-Borus, 2000, Lagana et al., 2002, Richardson et al., 2009, Miaskowski et al., 2011). Greater levels of pain in HIV/AIDS are associated with greater levels of psychological distress and lower emotional control (Rosenfeld et al., 1996, Rotheram-Borus, 2000, Lagana et al., 2002) and poorer quality of life (Breitbart et al., 1996)**.** Pain related symptoms in patients with HIV/AIDS include headache (51%), thrush (42%), painful joints (38%), muscle aches (37%), numbness (37%), abdominal pain (33%), chest pain (20%) and Kaposi's sarcoma lesions (19%) (Holzemer et al., 1998, Nicholas et al., 2010). In a prospective

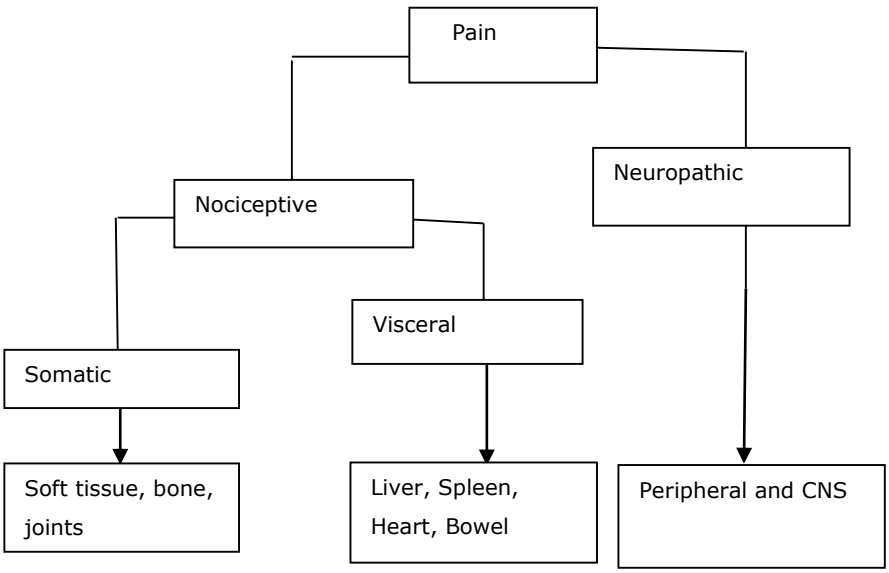
cohort study conducted in both rural and urban areas in the USA, oral pain, numbness of both lower and upper extremities, were associated with worst quality of life. Headache was associated with disability days (Lorenz et al, 2001). A systematic review reported that head, neck and lower limbs were the frequent anatomical sites pain is experienced by people living with HIV/AIDS (Parker et al., 2014). Multiple pains have been reported to be associated with increased disability and greater depressive symptoms (Breitbart et al., 1996). Physical pain is as a result of biological processes in the body. The feeling of pain itself causes psychological problems such as worry, anxiety, and hence the need for social care and support (Sepulveda et al., 2002).

Pain in HIV can interfere with every aspect of the patient's life (Newshan, 1997, Larue et al., 1997, Newshan and Sherman, 1999, McCormack et al., 1993). Since the severity of pain in HIV has been shown to increase with the progression of HIV disease, this produces greater interference in the performance of daily activities, decreases enjoyment of life and lowers mood levels (Mc Cormack et al, 1993; Singer et al, 1993). In a cross-sectional study conducted in India among 140 HIV/AIDS patients, two-thirds of HIV/AIDS patients reported that pain interfered with their mood, sleep, general activities, and abilities to perform normal work (Nair et al, 2009). In another cross-sectional study conducted in South Africa among a convenient sample of 100 hospitalised HIV/AIDS patients, it was reported that pain severity was strongly correlated with pain interference with daily life activity, mood, normal work, sleep and enjoyment of life (Narasimooloo el at, 2011).

3.5 Classification of pain

HIV-related pain is usually divided into two categories: nociceptive and neuropathic (Gray and Berger, 2007, Watson et al., 2009). Nociceptive pain is further sub-divided into somatic pain and visceral pain (Wentz, 2005, Watson et al., 2009). Somatic pain results from injury of structures such as muscles, skin, joints and bones. It is easy to locate and often experienced as throbbing and stabbing. Visceral pain is associated with distension of thoracic or abdominal organs such as liver or spleen and usually experienced as sharp and/or cramping (Watson et al., 2009). Some patients experience neuropathic pain as a result of opportunistic pathogens and side effects of drugs (Wentz, 2005, Lebovits et al., 1989). This pain causes injury to the peripheral and central nervous systems (Watson et al., 2009, Lebovits et al., 1989). Figure 4 summarises the classification of pain (Watson et al., 2009).

Figure 4 Classification of pain



3.6 Pain Assessment

Good pain management requires careful and proper assessment, but presents challenges due to the subjective nature of pain. Pain is a subjective phenomenon and as such it poses a challenge in terms of assessment (Steeds, 2009). Pain experts recommend routine pain assessment at each patient encounter such that pain assessment should be treated as part of the vital signs (Campbell and Mitchell, 1996). Pain assessment tools are available to assist in pain assessment and are based on the patient's own perception of their pain and its severity (Noble et al., 2005). Due to chronic nature of HIV/AIDS pain assessment requires a multidimensional approach (Marcus et al., 2000).

There is a consensus among experts that for palliative care patients, the five most important aspects of the pain experience which should be addressed by a pain assessment tool are:

- Pain intensity
- Temporal pattern
- Treatment and exacerbating / relieving factors
- Pain location
- Pain interference.

Other important aspects are pain quality, affective aspects of pain, the duration of pain, pain beliefs and pain history (Hølen et al., 2006, Caraceni et al., 2002b).

There are a number of pain measurement tools that have been validated for research and treatment of patients with chronic illnesses. The tool to

use depends on the factor of pain you wish to evaluate (Frampton and Hughes-Webb, 2011). To measure pain intensity and for on-going monitoring of pain intensity, a simple visual analogue scale and numerical rating scale is appropriate (Hølen et al., 2006).

There are three main ways to assess pain intensity and relief. These are through the use of visual analogue scale, a numerical rating scale, and a verbal rating scale. These are all well validated in cancer populations (Caraceni et al., 2002b), but there use may be extended beyond this to HIV/AIDS populations or those of other chronic illness (Watson et al., 2009). There is much debate as to the preferred method (Caraceni et al., 2002b, Brunelli et al., 2010) but a systematic review (Hjermstad et al., 2011) reported that the numerical rating scale has better compliance, is easier to use and has good acceptability compared to visual analogue scales and verbal rating scales.

The visual analogue scale (VAS) Figure 5a comprises a 10 cm line anchored by two verbal descriptors, one for no pain, the other one for severe pain (Hawker et al., 2011). Patients are asked to place a line perpendicular to the VAS at the point that represents their pain severity/intensity. A ruler is then used to measure the distance on the line as indicated by the patient. A higher score indicates greater pain severity.

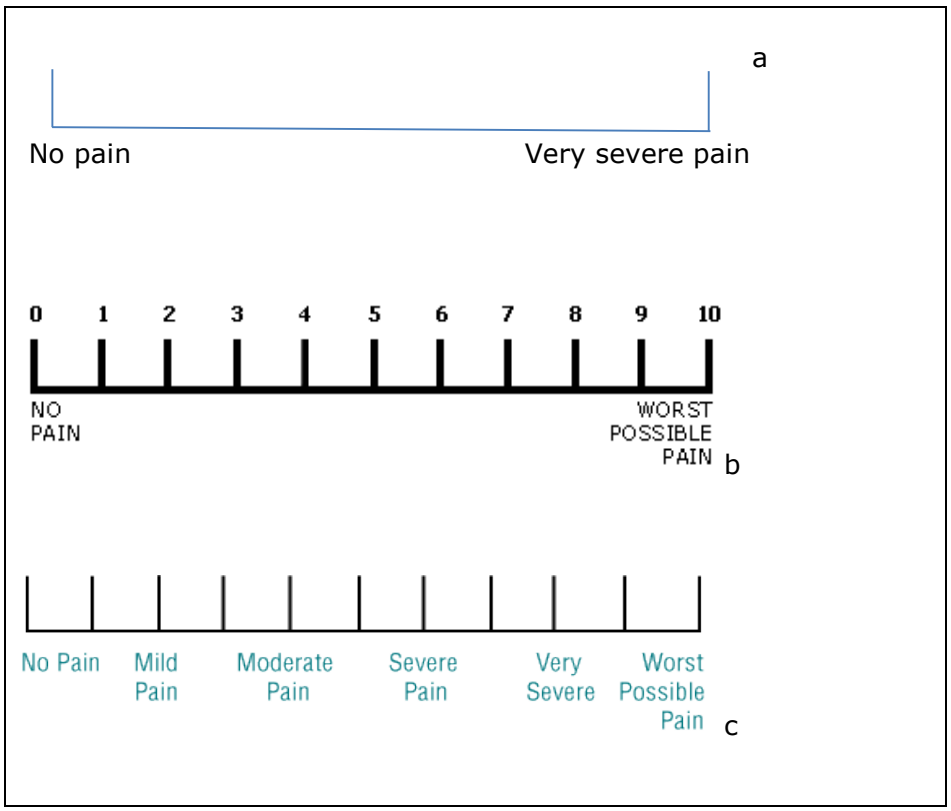
The Numerical rating scale consists of numbers from 0-10 Figure 5b. In this scale the intensity of pain increases as the numbers increase, patients are asked to indicate on the scale which number relates to the level of pain they are experiencing or have been experiencing (Frampton and Hughes-Webb, 2011). The numerical rating scale is easier to use (Hølen et al.,

2006), it measures pain intensity and relief both before and after treatment (Caraceni et al., 2002b, Hjermstad et al., 2008). Pain can be categorised as mild, moderate and severe on the numerical rating scale.

The verbal rating scale uses words describing pain as experienced by the patient. Patients are asked to indicate on the scale the words that best describe their pain (Figure 5c).

In principal based on the severity of pain the patient is prescribed drugs according to the WHO analgesic ladder. Pain assessment is therefore very important because it provides a basis for pain management (Caraceni et al., 2002a).

Figure 5 Pain rating scales



(Adapted from International Association for the study of pain)

a: Visual analogue scale

b: Numerical rating scale

c: Verbal rating scale

3.7 Pain Management

Pain management requires a multidimensional model approach (Marcus et al., 2000). The available clinical strategies need to be used to assess pain and available effective pharmacological and non-pharmacological interventions need to be utilised to effectively manage pain in HIV/AIDS

(Marcus et al., 2000). Experts recommended that non-pharmacological interventions should not be used as a substitute for effective pain relief and management (Foley, 1985).

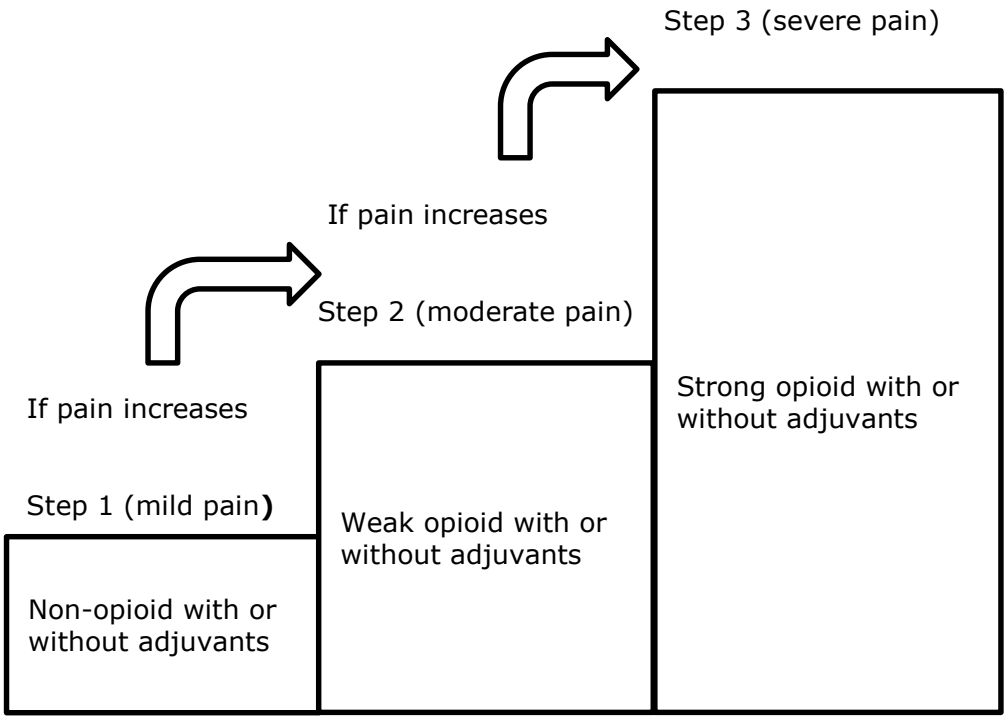
Pain relief should be seen as a vital component of HIV treatment. If painful side effects of antiretroviral drugs can be averted through effective pain control, people will be more inclined to adhere to their treatment (Clucas et al., 2011) and will be able to stop the replication of HIV far more effectively.

The WHO published guidelines for the pharmacological treatment and management of cancer pain in form of a ladder (Figure 6). These guidelines are referred to as the WHO analgesic ladder. The WHO analgesic ladder was developed in 1986 and validated among cancer patients (Ventafridda et al., 1987, Grond et al., 1991). Research has shown that those in severe pain can safely benefit from step 3 drugs from the start (Maltoni et al., 2005). Research has shown that in cancer patients 70-90% with pain treated according to the 3 step ladder achieves effective analgesia (Zech et al., 1995). The three steps WHO analgesic ladder (Figure 6) contains detailed information in terms of managing the pain and using appropriate drugs basing on the intensity and severity of pain.

Current evidence on pain management in HIV/AIDS patients is based on clinical experience and use of WHO analgesic ladder (Breitbart, 1996b, Newshan, 1995). Although the WHO analgesic ladder has not been validated in HIV/AIDS pain management, the guidelines on pain management in cancer or HIV/AIDS are not different (Frich and Borgbjerg, 2000), moreover treatment strategies for cancer pain has shown to be

beneficial in treating pain syndromes in HIV/AIDS (Ballantyne et al., 2009, Merriman, 2006).

Figure 6 WHO 3 steps analgesic ladder for pain management



(Adapted from WHO)

The figure above explains that if pain occurs, there should be prompt oral administration of drugs in the following order: Step 1 (mild pain): non opioids (for example Aspirin and Panadol); and if necessary jump to step 2 (moderate pain): mild opioids (for example Codeine); and if still necessary jump to strong opioids such as Morphine for severe pain, until the patient is free of pain (WHO, 2006b).

In order to relieve the patient from anxiety, fears and other social aspects of pain additional drugs, known as adjuvants are often used especially for neuropathic pain (Kieburtz et al., 1998, Simpson et al., 2010, Attal et al., 2010). However a systematic review and meta-analysis (Phillips et al., 2010) reported that all adjuvant drugs were not better than placebo, although some studies included in this review were shown to have serious methodological flaws (Kieburtz et al., 1998, Shlay et al., 1998).

It is important for patients to be kept free of pain, that analgesia is administered in an anticipatory way, regularly, around the clock, rather than on demand. This three-step approach of administering the right drug in the right dose at the right time is inexpensive and 80-90% effective (Jadad and Browman, 1995).

3.8 The need for pain relief in HIV/AIDS patients

In this section, I will hight the need for pain relief among HIV/AIDS patients. Freedom from pain is one of the important interventions in the provision of palliative care in HIV/AIDS.

HIV/AIDS patients report that they have several needs, among their needs are pain relief and management (Uwimana and Struthers, 2008). There are estimates that up to 80% of HIV/AIDS patients have their needs unmet (Grant et al., 2003, Harding et al., 2004b, Karus et al., 2005, Kikule, 2003, Sepulveda et al., 2002). WHO recommends that nations need to be committed to managing pain and other symptoms by training all health care workers and informing and educating the public (Stjernsward, 2002).

Other than pain relief, the predominant palliative care needs of HIV/AIDS patients are symptom management, psychological support, spiritual support, nutritional needs and financial support (Harding et al., 2004a, Coughlan, 2003). These needs are often not met (Sepulveda et al., 2003, Laschinger et al., Uwimana and Struthers, 2007) and where these needs are met it is mainly through the support of families and relatives (Sepulveda et al., 2003, Beedham and Wilson-Barnett, 1995).

In the next section, I will describe family carers of patients living with HIV/AIDS. I will explain the various roles and responsibilities family carers play, the challenges they experience, and the needs of family carers.

3.9 Carers of HIV/AIDS patients: defining carers

HIV/AIDS patients are mostly looked after at home by parents, a spouse, siblings, or any other relation or by friends. Other carers include community members providing voluntary care, that is without remuneration (Hudson and Payne, 2009b). Carers are lay people in a close supportive role who share the illness experience of the patient and who undertake vital care work and emotional support (Department of Health, 2008, Help the Hospices, 2008). Without this many patients will be unable to remain at home, but family carers often lack the information and skills to prepare them for such a role (Hudson et al., 2009, Oldham and Kristjanson, 2004).

The primary responsibility for the day to day management of pain and related symptoms often lies with the patient and family members (Hudson and Payne, 2009a). Caregiving is a great responsibility and sometimes

quite overwhelming for caregivers' (Thielemann, 2000). Patients are likely to spend more time with their family members in their communities, than with health care workers. In Malawi family members are involved in providing nursing care to the patients even in hospitals where staff shortages are common place. The majority of HIV/AIDS patients receive care in the ambulatory care setting with their primary care. Therefore it is imperative that primary carers are equipped with knowledge in the appropriate assessment, management of pain (Marcus et al., 2000). Family carers consistently identify pain management as their primary concern in relation to care and support of their loved ones at home (Oldham and Kristjanson, 2004). The challenges family carers experience in their day to day activities are discussed in the next section.

3.10 Challenges experienced by family carers

Family caregivers are crucial to health care systems, providing the majority of physical and emotional care for individuals with life-threatening and terminal illnesses including those who wish to die at home (Gomes and Higginson, 2006, Grande and Ewing, 2008, Rabow et al., 2004). Pain management is a particular concern of family carers looking after patients with chronic illnesses such as Cancer and HIV/AIDS (Oldham and Kristjanson, 2004, Pakenham et al., 2002).

Informal carers are central to the achievement of end of life care and death at home, they provide a substantial, yet hidden contribution to the economy (Grande et al., 2009, Butters et al., 1993, Help the Hospices, 2008). This is particularly the case in resource poor countries like Malawi.

Carers needs and the adverse effects of caring have been extensively researched, however there is little evidence to establish how these adverse effects may be prevented through appropriate support (Grande et al., 2009). These needs include psychological support, information, help with personal care, medication administration, respite, domestic and financial help (Aoun et al., 2005, Harding and Higginson, 2003). Care giving is associated with anxiety, depression, stress, strain, fatigue, and mortality (Ndaba-Mbata and Seloilwe, 2000, Chimwaza and Watkins, 2004, Kipp et al., 2007a, Kipp et al., 2007b). There is evidence of unmet need for information, financial and domestic support (Walsh et al., 2007, Mwinituo and Mill, 2006). It has been suggested that the needs of the carers often exceed those of the patients (Higginson et al., 1990, Payne, 1999). Although these studies were undertaken in non-HIV populations, challenges faced by carers may be similar.

Despite evidence of unmet needs and consistent calls in the literature for the development of tailored and specific services for carers such interventions have been rare (Harding et al., 2004a). In a systematic review there was found to be a considerable body of knowledge about the needs of carers, but little was identified and evaluated on the interventions and their effectiveness (Harding and Higginson, 2003).

A review of quantitative studies of family caregiving at the end of life from 1998–2008 identified the potential for negative emotional, psychological and physical outcomes for caregivers, as well as for financial strain and occupational and social disruption (Stajduhar et al., 2010). Caregivers' lack of preparation, knowledge and/or ability is a common finding, especially regarding symptom, pain, and medication management (Kazanowski,

2005, Armes and Addington-Hall, 2003, Oldham and Kristjanson, 2004). Family caregivers receive little preparation, information, or support to perform their care giving role (Hudson et al., 2008). However, their needs must be addressed so they can maintain their own health and continue to provide care (Northouse et al., 2010).

Family caregivers need education about pain management, training in problem-solving skills, and recognition from providers about their role in pain management (Oldham and Kristjanson, 2004). When clinicians better understand and respond to the needs of the family caregivers, they can enhance the quality of life and care outcomes for both patients and their caregivers (Meeker et al., 2011). The majority of patient care for HIV/AIDS is undertaken in patients' homes, as such the effectiveness of a patient's pain management is affected by the knowledge and attitudes of patients and caregivers (Ministry of Health, 2008b). The experience of caring for a family member in pain profoundly affects the caregiver's well-being, and the caregiver's effectiveness in helping with pain management affects the well-being of the patient (Meeker et al., 2011). If family carers do not feel confident and knowledgeable about pain assessment and management, patients may require more frequent hospital admissions and medical treatments. Carers who are unfamiliar with pain management may over or under dose patients with opioids (Oldham and Kristjanson, 2004).

The next section describes home-based care for people living with HIV/AIDS. People living with HIV/AIDS are looked after by family members in their own homes, and hence home-based care. This high prevalence rate has over stretched the health care system due to lack of resources, few number of hospital beds and limited number of health workers in the health

facilities. Most of the chronically ill patients go home when they are discharged while on-going care is still required. For this reason, home based care for chronically ill patients is one of the suitable interventions in the care and support for HIV and AIDS patients (Tapsfield and Bates, 2011; Wahab and Salam, 2011).

3.11 Home-based care

Home-based care is health care provided at home in the home by families, volunteers with support and assistance from health workers (Ndaba-Mbata and Seloilwe, 2000, Hudson and Payne, 2009a). In Malawi home-based care is defined as care provided to chronically, terminally ill patients with conditions such as cancer, stroke, HIV/AIDS and any other chronic illnesses, with the aim of restoring and promoting maximum health and comfort to the patient and family (National AIDS Commission, 2003, Ministry of Health, 2011b). Most patients with life limiting illnesses are cared for at home by their families in a familiar setting (Ministry of Health, 2011b, Ministry of Health, 2008b). It is estimated that 90% of the chronic illnesses including HIV/AIDS are managed in patient homes by untrained family carers (Ogden et al., 2006). Literature on care giving for patients with life limiting illnesses and their families suggests that families who receive detailed information and training about patient care manifest more vigilant coping compared with families who receive little or no information (Ndaba-Mbata and Seloilwe, 2000, Help the Hospices, 2008). In addition families who receive information about home health care activities, and challenges that may be experienced are less anxious and ready to receive

and give quality care to their loves ones (Derdiarian, 1986).

Home-based care is viewed as a cost effective response to managing the problems experienced by patients. However adequate training, resource supply and support is often neglected among family carers (Hunt, 2009). Less attention has been paid to the role of patient and carers in managing the patients pain despite the fact that HIV/AIDS pain is managed on an outpatient basis and in patients own homes (de Wit et al., 1997).

International health organizations such as (WHO, 1990) and the American Pain Society (Gordon et al., 2005), emphasise the importance of education on pain and the involvement of patients and carers in managing pain. However few studies have fully considered the importance of this involvement. There is shortage of health care workers in Malawi and other countries in SSA, and hence the need for home-based care (Grant et al., 2011). There are also few personnel trained in palliative care (Harding et al., 2003). Home-based care provides practical, emotional, physical and spiritual support to people in their own homes (Ministry of Health, 2011b).

Interventions for carers need to provide strong evidence for appropriate ways of supporting carers. Lack of a firm empirical and conceptual basis has prevented the design of effective interventions and the generation of evidence to demonstrate their impact (Grande et al., 2009).

3.12 Chapter summary

Pain remains a challenge in the population of HIV/AIDS patients and has negative effects on their quality of life. Pain is experienced throughout the

disease trajectory and it is more severe as the infection advances. Pain is also experienced due to the side effects of HIV treatment/medication. Currently with the advancement being made to improve the access to HIV drugs in resource poor countries, HIV patients are living longer, which means they will continue to experience pain throughout their life span. Provision of effective interventions to the population of HIV/AIDS patients is needed to minimise or reduce the severity of pain.

Home-based care and palliative care in HIV/AIDS patients is crucial in order to reduce the physical, social, psychological and spiritual problems that they experience. Family carers of HIV/AIDS patients play a crucial role in the implementation of home-based care and palliative care services particularly in Malawi.

The next chapter contains a critical review of randomised controlled trials evaluating the effects of pain education interventions among patients with HIV/AIDS.

CHAPTER FOUR: A REVIEW OF EVIDENCE FROM RANDOMISED CONTROLLED TRIALS OF EDUCATION INTERVENTIONS ON PAIN AND SYMPTOM MANAGEMENT FOR HIV/AIDS PATIENTS

4.1 Introduction

This chapter provides a detailed review of literature of published studies on the effects of educational interventions on pain severity and pain management from previous randomised controlled trials. The chapter contains the process of conducting the review, inclusion and exclusion criteria for the studies, and methodological quality assessment of studies. In addition, the presentation of findings from the review, and gaps in literature. Although there is evidence that pain education interventions have positive effects in reducing the severity of pain, improving knowledge and quality of life among people living with HIV/AIDS, little is known about their effectiveness in sub-Saharan African contexts. This review critically appraises available evidence reported in randomised controlled trials with two or more parallel groups.

This review focuses on pain and education because palliative care nurses play a crucial role of educating patients on pain management. Being a palliative care nurse one of my roles was to educate patients and families on management of pain.

4.2 Defining a systematic review

A systematic review is a process which locates, appraises, and summaries evidence from available studies pertinent to a specific question by using an explicit, logical and scientific methodology (Khan et al., 2011). Systematic reviews are scientific investigations in themselves, with pre-planned methods and an assembly of original studies as their "subjects." (Cook et al., 1997). They synthesize the results of multiple primary investigations by using strategies that limit bias and random error (Cook et al., 1995). These strategies include a comprehensive search of all potentially relevant articles and the use of explicit, reproducible criteria in the selection of articles for review. Primary research designs and study characteristics are appraised, data are synthesized, and results are interpreted (Cook et al., 1997, Mulrow et al., 1997).

Typically in a systematic review, a clinical problem is considered, evidence evaluated and synthesised so that conclusions can be drawn about effective practices. A systematic review is not a literature review; it is a methodology of conducting research in itself (Polit and Beck, 2008). It brings together and assesses all relevant research evidence to provide answers to a particular research question (Evans, 2001, Evans and Pearson, 2001). It adheres to a rigorous scientific design to minimise the risks of biases and ensure reliability (Cook et al., 1997). This is contrary to traditional literature review methods which are conducted without formal guidance rules. Such reviews tend to be subjective. Furthermore, traditional reviewers are rarely explicit about how studies are selected, assessed and integrated (Davies and Crombie, 2001) and the risk of

publication bias is increased (Webb and Roe, 2007, Spector and Thompson, 1991).

Traditional reviews are not always rigorous; reviewers rarely begin with an open mind as to the likely recommendations (Davies and Crombie, 2001). Traditional reviews deal with a broad range of issues related to a given topic rather than addressing a particular issue in depth (Mulrow et al., 1997), thus they are useful in obtaining a broad perspective on a topic, they are less often useful in furnishing quantitative answers to specific clinical questions (Cook et al., 1997) while systematic reviews are generated to answer specific, often narrow clinical questions in depth (Richardson et al, 1995).

Systematic reviews overcome these weaknesses of traditional narratives by making the review process transparent (Newman and Fleming, 2002). In adequately presented systematic reviews, they allow readers to replicate the review and are more objective (Egger, et al, 2001). Systematic reviews have increasingly replaced traditional reviews as a way of summarising evidence for effectiveness of diagnostic and treatment interventions (Collins and Fauser, 2005). Systematic reviews of randomised controlled trials are considered to be evidence of the highest level in the hierarchy of research designs evaluating effectiveness of interventions (Akobeng, 2005b, Evans, 2003).

Following an extensive literature search I found no evidence of recent systematic review to bring together evidence from published randomised controlled trials on pain management among people with HIV/AIDS and family carers. Recent systematic reviews of home palliative care services

for people with advanced illnesses and their caregivers have focused on a number of chronic illnesses such as congestive heart failure and chronic obstructive pulmonary disease (Gomes et al., 2013). Another recent systematic review on self-management education programs for people living with HIV/AIDS included studies conducted in western countries, excluding all studies conducted in Africa. The study concluded that self-management education interventions have short-term effectiveness in improving physical, psychosocial, and knowledge among people living with HIV/AIDS, but no sufficient evidence on long-term effects of the interventions (Millard et al., 2013).

4.3 Aims and objectives of the review

The aim of this review was to examine and update the synthesised evidence regarding the effect of pain education interventions on a range of patient outcomes. The review sought to specify the contents and form of existing pain education interventions for people living with HIV/AIDS.

4.4 Objectives

The objectives of the review were to:

- Identify educational interventional studies of pain assessment and management for HIV/AIDS patients.
- Identify the educational interventional strategies used in managing pain.
- Identify pain, education, and quality of life outcomes among people living

with HIV/AIDS.

There many interventions that are used to manage pain which include psychological, respite care, coping skills, cognitive behavioural therapy and educational interventions. I chose studies that focused on educational interventions because one of my roles as a palliative care nurse is to provide education to patients and family members. Education interventions are feasible and easier to design and implement in Malawian context.

4.5 Search strategy

A comprehensive search strategy was developed and utilised to identify relevant studies published in English language only. The following data bases were searched: Amed, Assian, CINAHL, Cochrane Library, EMBASE, MEDLINE, PsycINFO and Web of Science from 1984 to February 2014, because HIV was first reported in 1983. The following key words or subject headings were used: HIV, AIDS, pain assessment, pain management, and pain education (Table 3).

As randomised controlled trials is the suitable methodology of evaluating interventions, therefore "randomised controlled trials" was used as a key word in the title, abstract, and content (full text) was used to map quantitative evidence.

All articles were screened and duplicates were deleted. Hand search was also used by going through the reference list of articles of the identified studies that investigated the effect of pain education interventions on people living with HIV/AIDS and/or family carers.

Table 3 Search terms used

Key concepts	Key words
HIV	HIV, human immune deficiency virus
AIDS	AIDS, Acquired immune deficiency syndrome
Pain education	Patient education, patient teach, patient learn, patient inform, pain knowledge
Pain management	Self-management, pain, symptom, management
Research methodology	Randomised controlled trial

4.6 Inclusion and Exclusion criteria

4.6.1 Inclusion criteria

Studies were included if they were:

- Randomised and non-randomised controlled trials
- Evaluated educational interventions of any form.
- Compared educational intervention with usual care/standard care.
- HIV/AIDS patients were participants

4.6.2 Exclusion criteria

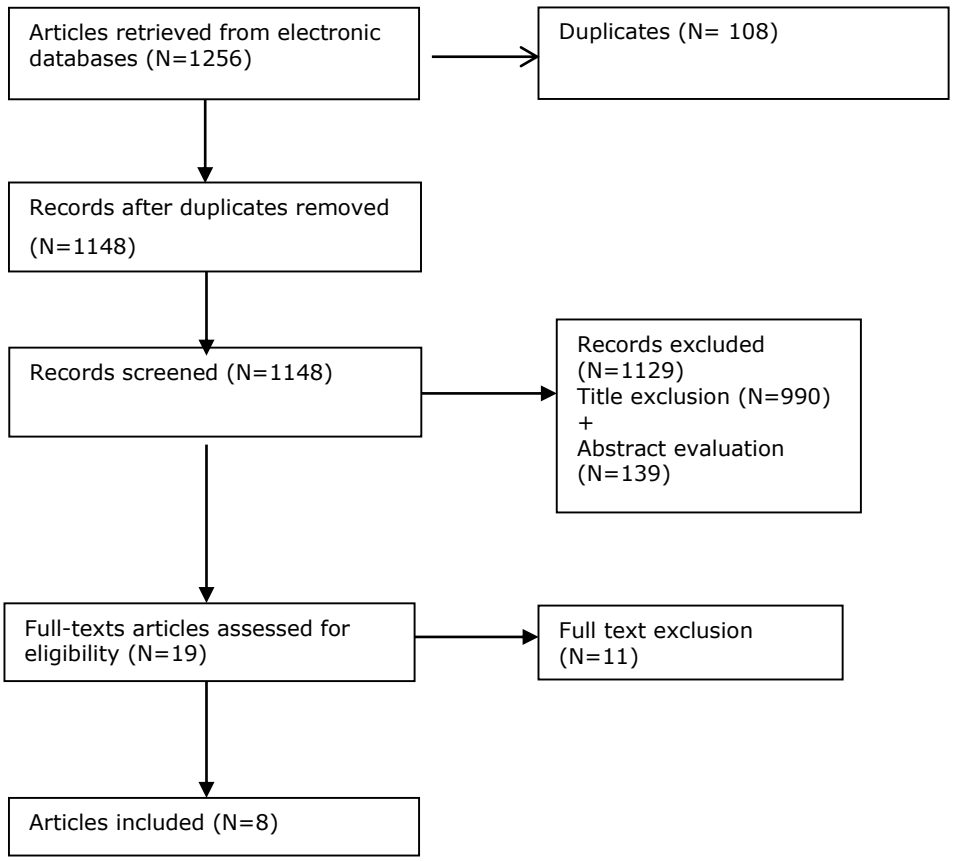
Studies were excluded if they were:

- Non educational interventions such as psychosocial interventions.

Table 4 Summary of Inclusion criteria

	Inclusion
Type of participants	Patients with HIV/AIDS
Type of studies	Randomised controlled trials Non-RCT Quasi experimental studies.
Type of intervention	Any Educational interventions of any form like leaflet, booklet, DVD, tape recording on pain assessment and management. Psycho-educational interventions were also included.
Outcomes	Pain intensity/severity, symptom intensity/severity, pain interference, pain knowledge, quality of life.

Figure 7 PRISMA flow chart of study selection process



4.7 Studies identified

The full text of 1256 articles were obtained from electronic data bases through a comprehensive search. All articles were discarded if they were duplicates (N=108) and after reviewing the title of the articles (N=990). Abstracts were then reviewed and other studies were also excluded (N=140) because they did not meet the inclusion criteria (Figure 7). Consequently the final articles which meet the inclusion criteria were obtained for evaluation (N=18). After full text extraction ten studies were excluded because the intervention was psychosocial, drug adherence, cognitive-behavioural therapy, and depressive symptoms. Summary of all studies included in the review are presented in the table 7.

4.8 Methodological quality of the trials

All the eight studies included in the review were critically evaluated on a checklist recommended by the Centre for Review and Dissemination (Centre for Review and Dissemination, 2009) and Critical Appraisal Skills Programme (Critical Appraisal Skills Programme, 2013) for evaluating randomised controlled trials (Table 5 check list for assessing validity of randomised controlled trials) and Quality assessment for all studies are summarised on Table 6.

Table 5 check list for assessing validity of randomised controlled trials

Item No.	Topic	Checklist item
1	Randomisation	Was the assignment to treatment groups really random?
2	Blinding of participants and researchers	Were participants blinded to treatment groups? Were health care workers blinded to treatment groups?
3	Baseline similarity	Were the intervention and control groups similar at the start of the trial?
4	Identical except intervention	Aside from the intervention were the groups treated equally?
5	Blinding of outcome assessors	Were those assessing outcomes blind to the treatment groups?
6	Follow-up	Was relatively completed follow-up achieved?
7	Analysis of data	Was ITTA or modified ITTA performed? Were the outcomes of the participants who withdrew described and included in the analysis?

4.9 Description of the studies

Participants in general were not blind to group allocation though this was not stated clearly in two of the nine studies (Wantland et al., 2008, Webel, 2010). Given the nature of non-pharmacological interventions, blinding was not feasible and this has potential to raise performance bias among participants in self-reported outcomes. The sample size ranged from 40 (Inouye et al., 2000) to 775 (Wantland et al., 2008) participants. In all of the nine studies random allocation was performed effectively. One study (Lechner et al., 2003) reported that outcome assessors were blind to participant group allocation and two studies reported that participants self-completed the questionnaires (Wantland et al., 2008, Gifford et al., 1998), however the rest did not report who conducted follow-up outcomes and whether they were blind or not.

In general participants were broadly similar at baseline, however two studies (Wantland et al., 2008, Inouye et al., 2000) did not clearly report this. Of the nine studies reviewed, five achieved 80% follow-up rate. One study reported 34.6% attrition (Wantland et al., 2008). One study did not clearly state how many participants were lost to follow-up (Inouye et al., 2000). Two studies followed-up all the participants they recruited and performed intention-to-treat analysis (Chiou et al., 2006a, Chiou et al., 2004). Two studies performed modified intention-to-treat analysis, they excluded all participants who were lost to follow-up (Lechner et al., 2003, Gifford et al., 1998). In one study missing subscales from questionnaires were replaced with group means, but missing data due to lost to follow-up was not replaced (Lechner et al., 2003). In one study, some participants in the control group deviated from the protocol, they received the intervention despite being randomised to control group, however the authors did not explain if they performed per protocol analysis or modified intention-to-treat analysis (Goujard et al., 2003). One study included participants lost to follow-up in the final analysis (Webel, 2010). Two studies (Wantland et al., 2008, Inouye et al., 2000) did not report if they included or excluded participants lost to follow-up in the analysis. All studies provided information about characteristics and reasons for lost to follow-up. Excluding study participants who withdrew from the study after sustaining severe side effects to the intervention will affect the results of the trial and has potential to introduce bias (White et al., 2011, Abraha and Montedori, 2010, Ellenberg, 2005).

Table 6 Quality assessment of the RCTs included in the review (N=9)

Studies	Random allocation	Blinding of patients	Analysis of withdrawal	Assessor blinded?	Groups comparable at baseline	Identical except intervention	Complete follow-up	Overall quality
Goujard et al (2003)	Yes	No	Withdrawals not included, but not clear if ITTA or per protocol analysis	Not stated	Yes	Yes	80% complete follow-up	4/7
Wantland et al (2008)	Yes	Not stated	Not stated	Self-completed by participant	Not clear	Yes	No, 34.6 % attrition rate	3/7
Luchner et al (2002)	Yes	No	Modified ITTA, withdrawals excluded	Yes	Yes	Yes	80% completed follow-up	5/7
Gifford et al (1998)	Yes	No	Modified ITTA	Self-completed by participant	Yes	Yes	81% complete follow-up	5/7
Chiou et al (2004)	Yes	No	N/A	Not stated	Yes	Yes	Yes	4/7
Chiou et al (2006)	Yes	No	N/A	Not stated	Yes	Yes	Yes	4/7
Inouye et al (2000)	Yes	No	Not stated	Not stated	Not clear	Yes	Not clear	2/7
Webel et al (2010)	Yes	Not stated	Yes	Not clear	Yes	Yes	80% completed follow-up	5/7

In table six above, only three of the eight studies included in the review were of good quality, with a score of five out of seven (5/7).

4.10 Nature of Interventions

In this section the nature of interventions tested is described. The section also contains a highlight of the type of education intervention tested, who delivered the intervention, how the intervention was deliverd, for how long, and how the intervention differs from usual care provided.

A full description of the interventions tested are summarised in table 7. Broadly the nature of the interventions were similar. They were all educational interventions provided to patients infected with HIV/AIDS., peer educators (Gifford et al., 1998, Webel, 2010) or self-managed by the patients (Chiou et al., 2004, Chiou et al., 2006a, Lechner et al., 2003, Wantland et al., 2008, Goujard et al., 2003). Some interventions were provided to patients in groups (Lechner et al., 2003, Chiou et al., 2004, Chiou et al., 2006a). All the studies had two parallel groups, the intervention and usual care; except (Chiou et al., 2004, Chiou et al., 2006a), these had three parallel groups. There were two interventions delivered either to patients as individuals (one-to-one teaching) or patients were in groups which meant interaction among group members, and the control group received usual care only (Chiou et al., 2006a), however in a related study (Chiou et al., 2004) the control group received usual care and telephone counselling .

Two studies (Webel, 2010, Lechner et al., 2003) tested two different interventions. One tested the effects of a group-based cognitive-behavioural stress management/expressive-supportive therapy compared with a time-matched individual psycho-educational therapy (Lechner et al., 2003), another tested a peer-based symptom management intervention

compared with a self-management symptom manual (Webel, 2010). The interventions focused on self-assessment of symptoms (Wantland et al., 2008, Gifford et al., 1998, Inouye et al., 2000) and self-management of symptoms of HIV/AIDS infection or side effects of HAART (Wantland et al., 2008, Inouye et al., 2000, Chiou et al., 2004, Chiou et al., 2006a, Gifford et al., 1998). Skills training (Inouye et al., 2000, Chiou et al., 2004, Chiou et al., 2006a, Gifford et al., 1998), promotion of drug adherence and improving knowledge levels (Goujard et al., 2003), psycho-educational intervention (Lechner et al., 2003). Four studies provided educational materials to the participants such as a symptom management manual (Wantland et al., 2008, Webel, 2010) and/or a video (Lechner et al., 2003, Inouye et al., 2000).

Five studies invited participants randomised to the control groups to receive the intervention upon completion of follow-up assessments (Inouye et al., 2000, Chiou et al., 2004, Chiou et al., 2006a, Gifford et al., 1998, Goujard et al., 2003).

In the trial conducted by Inouye et al (2000) participants in the intervention group received self-management training and education for seven weeks, the intervention was administered twice a week, and participants attended a total of 14 sessions, each lasting 60-90 minutes. However the authors did not report who facilitated the training education. Participants in the control group received usual care provided by their primary care providers, and received the intervention upon completion of follow-up assessments (Inouye et al., 2000).

In two of the five studies with a wait-list control group (Chiou et al., 2004, Chiou et al., 2006a) both studies had two treatment groups consisting of one-to-one teaching and group teaching on symptom management programme once a week followed by three weeks continuity and telephone counselling. The control group participants received usual care and were invited to receive the intervention upon completion of follow-up assessments. However in one of these two studies the control group received telephone counselling intervention like other two parallel treatment groups (Chiou et al., 2004).

In another study, participants randomised to the intervention group were taught self-management skills of HIV/AIDS symptoms using various means such as role playing, information sharing and problem solving skills. This was a group based intervention facilitated by peer leaders. Participants who were randomised to the control group received usual medical care and were invited to participate in the self-management education programme after three months of follow-up assessments (Gifford et al., 1998).

In another study, participants randomised to the intervention group received an individualised educational programme focussing on drug adherence. Participants in the control group were invited to participate in the education programme after 12 months of follow-up assessments (Goujard et al., 2003).

In a trial conducted by (Wantland et al., 2008) participants randomised to the intervention group were provided with a symptom management manual which focuses on description of HIV/AIDS symptoms, ways of treating the symptoms and self-care strategies that may be useful to

decrease and resolve the symptoms. Participants in the control group received a manual on HIV/AIDS nutritional guidelines.

Two of the eight studies did not have a usual care control group. They compared the effects of two different interventions (Lechner et al., 2003, Webel, 2010). In one of these two studies (Lechner et al., 2003) participants in one experiment group received a group-based cognitive-behavioural stress management/expressive-supportive therapy while participants in the other experiment group received a time-matched video-based individual psycho-education. In another study, one intervention group attended a self-management skills programme (Webel, 2010) based on the previous work (Gifford et al., 1998) on peer education on symptom management, although (Gifford et al., 1998) recruited men only, and (Webel, 2010) recruited women only. The study (Webel, 2010) compared the peer education intervention (Gifford et al., 1998) to the symptom management manual (Wantland et al., 2008) among women living with HIV/AIDS.

Table 7 Summary of RCT Studies included in the review

Author/Setting	Sample	Intervention(s)	Comparator	Outcomes/measures	Results
Inouye, et al (2000) in the USA	40 patient participants (20 randomly allocated into two groups)	Seven week program of self-management training and education provided twice a week	Usual care (details not provided), but also received the intervention after completion of follow-up assessments.	1.Physical health status: number of physical symptoms; Karnofsky performance scale (KPS) and CD4 count after seven weeks 2. Quality of life (QOL): quality of life index (QLI) after seven weeks	1.No significant differences on mean number of symptoms and CD4 count 2.No significant effects on quality of life
Gifford et al (1998) USA: San Francisco bay settings.	71 men with HIV/AIDS symptoms: (34 experimental group; 37 control group) randomly allocated to groups.	Interactive health education group session; 7 sessions in total about self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition facilitated by 2 peer leaders.	Waiting list and received usual care.	1.Symptom severity assessed with a 14-item symptom severity index 2.Pain was assessed with 5-item Medical Outcomes Study 3. HIV knowledge was assessed with a 10-item HIV knowledge created for this study. All outcomes were assessed at three months.	1. Symptom severity decreased in the experiment group and increased in the control group (-0.9 versus +0.5; p <.03). 2. There were no significant differences in pain outcome between the intervention and groups. 3. control group showed a better knowledge improvement compared to intervention group.

Author/setting	Sample	Intervention(s)	Comparator	Outcomes/measures	Results
Chiou et al (2004) in Taipei (STD control centre, medical centre and Catholic AIDS support)	67 participants: 23 in the individual teaching group, 22 in the group teaching group and 22 in the usual care group	One-to-one teaching attended a 60 minute teaching program on HAART side effect, safe care education and skill training weekly, for 3 weeks and telephone counselling Group teaching, as above except it was a 90 minute program	Usual care and telephone counselling. Received the intervention after follow-up assessments.	1.Medication side-effects safe care knowledge assessed with medication side effects self-care knowledge questionnaire (MSSKQ) 2.self-esteem (Rosenberg's self-esteem scale) 3. Unscheduled hospital visits (UHV). All outcomes were evaluated after 3 months.	1. Knowledge of management of medication side effects in the teaching groups was statistically significant compared to the control group (P<0.001). 2. No statistically significant differences between the three groups on self-esteem. 3. Unscheduled hospital visits: one-to- one teaching group P=0.017; individual teaching group P=0.035; usual care group P=0.655.
Lechner et al (2002) Miami-Dade County, Florida, New York and New Jersey (USA)	330 women randomly assigned to two treatment groups	Group-based cognitive-behavioural stress management/expressive-supportive therapy (CBSM) for 10 weeks (two hour, weekly sessions) (n=150)	Time-matched videotape-based individual psycho education two hour weekly sessions for 10 weeks (n=180).	1.Quality of life assessed with the Medical Outcomes Study Health Status Questionnaire for HIV (MOS-HIV-30) after ten weeks 2. CD4 and CD8 lymphocyte counts; HIV viral load after ten weeks.	1. QOL scores increased in both groups, but scores were statistically significantly higher in the CBSM group 2. No significant differences in CD4, CD8 and HIV viral load.

Author/setting	Sample	Intervention	Comparator	Outcomes/measures	Results
Chiou et al (2006) Taipei medical centre, STD control centre, and AIDS social service agency	67 participants: 23 were on one-on-one teaching; 22 in teaching group; 22 in control group	Symptom management instruction in self-care of the symptoms caused by side effects, skill training and telephone counselling for three weeks	Control group received usual care (details not provided), and received the intervention after conclusion of data collection	1.Drug adherence measured with The Customised Adherence Self-Report Questionnaire 2.CD4 count and viral load 3.Quality of life (QOL) measured using QOL index All outcomes were evaluated after three months.	1.Mean differences on the Customised Adherence Self-Report Questionnaire were statistically significant in the experiment groups compared to the control group 2.CD4 count and viral load were significant in both experiment groups compared to the control groups 3.QOL in both experimental groups were statistically significantly better than in the control group
Webel (2010) San Francisco Bay (USA)	89 women	Seven, two-hour peer-led sessions over seven weeks Interactive health education group session; 7 sessions in total about self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition facilitated by 2 peer leaders.	Copy of symptom management strategies (Wantland et al, 2008)	1.Symptom intensity measured with the revised version of the HIV Sign and Symptom Checklist 2.Medication adherence assessed with the revised AIDS Clinical Trials Group 3. Quality of life assessed with the HIV/AIDS Targeted Quality of Life Instrument. All outcomes were assessed at week 14.	No statistically significant differences between the two groups in all outcomes.

Author/setting	Sample	Intervention	Comparator	Outcomes/measures	Results
Goujard et al (2003) France.	367 HIV patients (179 control and 188 experiment).	Individualised educational programme based on diagnosis of adherence problem to HIV medication. It used planning card with self-adhesive stickers showing treatment medication, followed by at least 1 hour educational sessions for 12 months. Staff nurses and physicians facilitated the program.	Standard care (no details provided). Participants were invited to attend the education programme upon completion of follow-up assessments.	1.Knowledge about HIV and its treatment assessed with the 14 item knowledge questionnaire 2. Adherence to medication (PMAQ7) 3.QOL (HIV-46) 4. Therapeutic response (CD4 count and viral load). All outcomes were assessed at six, 12 and 18 months.	1. Knowledge score increased at 6 months, 12, 18 in both groups, with a higher improvement in the experimental group at 6 and 12 months. 2. Significant differences between the intervention and control groups on adherence score at 6, 12 and 18 months. 3. QOL scores increased in the experimental group over time, but no significant differences between the two groups. 4. No significant differences on CD4 count and viral load between the two groups.
Wantland et al (2008) Africa, Puerto, 10 sites across USA.	775 HIV patients recruited from community clinics.	Experimental group received a manual on symptom management.	Control group received a manual on general nutrition.	Frequency and intensity of HIV symptoms at baseline, 1 month and two months follow ups: Revised Sign and Symptom Checklist for persons with HIV disease (SSC-HIV).	Analysis showed a greater decline in symptom frequency and intensity for the experimental group compared to the control group (t=2.36, P=0.018).

Due to the heterogeneity of the interventions and populations studied meant that a meta-analysis was not appropriate and may give misleading/spurious findings. Ideally only controlled trials with proper randomisation of patients preferably blinded, outcome assessment with strict intention-to-treat principle should be included in the meta-analysis. The studies in this systematic review had methodological challenges.

4.11 Outcome measures

This section outlines the outcomes of interests in the studies reviewed.

Each study included had a variety of outcomes. Broadly the outcomes measured in the studies were pain severity, symptom frequency and intensity, quality of life, knowledge of pain management and medication side effects, and palliative care outcomes.

Some outcomes were self-reported by the participants and were evaluated using questionnaires, while some outcomes were clinical outcomes such as CD4 count, viral load, and unscheduled hospital visits.

The outcomes in the eight studies reviewed were measured using validated instruments. The outcomes in the studies are in line with IMMPACT recommendations on the main outcomes of interests in studies on pain interventions.

4.11.1 Pain and symptom outcomes

Only one of the eight studies examined pain score following the administration of the intervention (Gifford et al, 1998). In this study pain outcome was measured using the Medical Outcomes Study (MOS) pain severity scale (Gifford et al., 1998). The authors reported that there was no significant difference between the intervention and control groups after three months of follow-up assessments.

Four of the eight studies assessed HIV symptom severity (Gifford et al., 1998, Webel, 2010, Inouye et al., 2000, Wantland et al., 2008). In the trial by Gifford et al (1998), symptoms were measured and summarised using a 14-item symptom severity index to evaluate the overall burden caused by HIV symptoms. The symptom severity index decreased significant in the intervention group, compared to the control group after three months of follow-up assessments (Gifford et al., 1998). In another study HIV symptom intensity was evaluated with the HIV Sign and symptom check list, which identifies 72 common symptoms experienced by people infected with HIV. The questionnaire was administered at 2, 6, 10 and 14 weeks after delivery of the intervention. The study found no significant differences in symptom severity between the intervention and control groups (Webel, 2010). In another study physical symptoms were categorised into either high or low symptoms within each of the two groups. Participants with many symptoms were categorised as "high" and those with a few symptoms were categorised as "low". Physical symptoms were evaluated using the Karnofsky performance scale (KPS). The intervention found significant effects with the number of symptoms reported

after seven weeks of follow-up assessments (Inouye et al., 2000).

The symptom management manual study (Wantland et al., 2008) evaluated the frequency and intensity of HIV symptoms using The Revised Sign and Symptom Checklist for Persons with HIV Disease (SSC-HIVrev). The questionnaire was administered at baseline, month 1 and month 2. The trial reported that symptom frequency and severity significantly declined in the intervention group compared to the control group (Wantland et al., 2008).

In this review there was only one study (Gifford et al, 1998) that examined pain as an outcome, and four studies examined symptom severity (Gifford et al, 1998; Inouye et al, 2000; Wantland et al, 2008; Webel, 2010) (see Table 8). This suggests that few educational interventional studies in the field of HIV/AIDS have been conducted that evaluate the effects on pain related outcomes.

4.11.2 Quality of life outcomes

All studies included in the review evaluated quality of life outcomes except (Wantland et al., 2008, Chiou et al., 2004, Gifford et al., 1998). However quality of life was assessed using different measures and findings were not consistent.

Two studies of the nine studies (Webel, 2010, Goujard et al., 2003) concluded that educational interventions had no effect on quality of life. One study (Goujard et al., 2003) evaluated quality of life using HIV-46 questionnaire and

reported that the educational intervention on adherence to HIV medication lead to improved quality of life, but there was no significant difference between the experiment and control groups at 6,12 and 18 months, likewise (Webel, 2010) assessed quality of life using the HIV/AIDS Targeted Quality of life. The Target Quality of Life is a 34-item instrument measuring nine dimensions of HIV disease-specific quality of life. The study reported that there were no significant differences between the intervention and the control group at 10 and 14 weeks of follow-up assessments. (Webel, 2010). However, three of the nine studies found significant effects of educational interventions on quality of life (Inouye et al., 2000, Lechner et al., 2003, Chiou et al., 2006a).

Quality of life was assessed with Quality of Life Index (QLI) at baseline (Inouye et al., 2000, Chiou et al., 2006a), seven weeks (Inouye et al., 2000) and three months (Chiou et al., 2006a) after delivery of the intervention. Self-management programme significantly increased quality of life among HIV/AIDS patients who received the intervention compared to the patients who did not receive the intervention (Inouye et al., 2000). The study (Chiou et al., 2006a) had three parallel groups. There were two intervention groups. One intervention group was delivered on one-to-one or individual basis and the other intervention was delivered on group basis). The third group was a control group. The study concluded that participants in the two experiment groups experienced significant quality of life outcomes compared to participants in the control group (Chiou et al., 2006a).

Another study had two intervention groups with no control group. One

intervention group was a group-based, while another intervention group was individual-based. Quality of life was assessed with Medical Outcomes Study Health Status Questionnaire for HIV (MOS-HIV-30). Both interventions were reported to be effective in improving certain aspects of quality of life, although the group-based intervention experienced greater and statistically significant improvement in quality of life related to mental health aspect (Lechner et al., 2003).

Table 8 Outcomes of pain education interventions among people living with HIV/AIDS

Studies / **Outcomes**	Gifford et al (1998) (n=71 men)	Inouye et al (2000) (n=40)	Lechner et al (2002) (n=330 women)	Goujard et al (2003) (n=367)	Chiou, et al (2004) (n=67)	Chiou et al (2006) (n=67)	Wantland et al (2008) (n=775)	Webel (2010) (n=89 women)
Physical and social								
Pain	=							
Symptoms	↓	↓					↓	=
quality of life		↑	↑	=		↑		=
Knowledge	=			↑	↑			
Self-esteem					=		↑	
Physiological								
CD4		=	=	=		↑		=
CD8			=					
Viral load		=	=	=		↓		=
Other								
Unscheduled hospital visit					↓			

=: No difference between two groups

↓: Significant decrease in the intervention group

↑: Significant increase in the intervention group

Table 8 above shows that only one study (Gifford at al, 1998) measured pain as an outcome and the results were not statistically significant.

4.11.3 Knowledge outcomes

Knowledge outcomes were assessed in three of the nine studies reviewed (Chiou et al., 2004, Goujard et al., 2003, Gifford et al., 1998). Two studies reported that education intervention improved knowledge (Chiou et al., 2004, Goujard et al., 2003) while one study reported that the education intervention did not improve knowledge levels (Gifford et al., 1998).

One trial (Chiou et al., 2004) assessed participants knowledge on HIV medication side effects and how to manage them using the Medication side effects self-care questionnaire (MSSKQ). The trial found statistically significant improvement in the knowledge of medication side effects and their management in the intervention compared to the control groups after seven weeks of follow-up assessments (Chiou et al., 2004). In another study knowledge levels were assessed with HIV knowledge questionnaire. Although the study reported that knowledge score increased in both groups with higher improvements in the intervention group, it is not clearly reported whether this improvement was statistically significant between the two groups (Goujard et al., 2003). On the contrary another study (Gifford et al., 1998) assessed knowledge using a 10-item HIV knowledge questionnaire specifically related to information with this study. Participants in the control group reported a greater knowledge improvement than participants randomised to the intervention group (Gifford et al., 1998), however they did not report whether this result was statistically significant between the two groups.

4.11.4 Self-esteem outcomes

Two studies (Wantland et al., 2008, Chiou et al., 2004) evaluated the effects of the intervention on self-esteem. The symptom management manual study evaluated the usefulness of the symptom management and nutritional management manuals. They reported that for both the experiment and control groups, individuals who rated the manuals very helpful at one and two months of follow-up assessments were significantly more likely to have lower symptom intensity scores that decreased rapidly over time compared to those who rated the manuals lower, suggesting the manuals were viewed to have a positive impact on the patients in decreasing the severity of the symptoms (Wantland et al., 2008).

In another study self-esteem was evaluated using Rosenberg's Self-esteem Scale (RSES). The intervention group a one-to-one or group teaching on self-care management skills of HAART side effects and telephone counselling. The comparison group received telephone counselling only. They found no significant differences between two groups at week seven after the delivery of the intervention (Chiou et al., 2004).

4.11.5 Other outcomes

Other outcomes reported in the studies were effects of the interventions on therapeutic response, by evaluating for example viral load levels, CD4 count and number of unscheduled hospital visits. Because these are not patient

reported outcomes, I wanted to see if the interventions delivered had an effect on the immune system bearing in mind that this is also another way to evaluate quality of life. CD4 count and viral load were evaluated in five of the nine studies (Inouye et al., 2000, Lechner et al., 2003, Goujard et al., 2003, Chiou et al., 2006a, Webel, 2010). Broadly the authors reported similar findings.

The self-management training and education programme study found no significant differences between the intervention and control group in CD4 cell count after seven weeks (Inouye et al., 2000). Likewise another study reported that there were no significant differences in CD4 cell count and viral load between the intervention and control groups after 14 weeks of follow-up assessments (Webel, 2010). Another study also found no significant differences in CD4 and CD8 lymphocytes counts and HIV viral load after four weeks of follow-up assessments (Lechner et al., 2003).

Although another trial reported that there was no direct effect of the educational intervention on CD4 cell count and viral load, there were increased levels of CD4 cells and decreased levels of viral loads in the intervention group compared to the control groups after 6 months following the delivery of the intervention. The trend was also confirmed after 12 months (Goujard et al., 2003). On the contrary the symptom management programme (Chiou et al., 2006a) found statistically significant differences in CD4 counts cells and viral load between the two experiments groups and one control group. Participants who were randomised to two experiment groups had increased CD4 cell counts

and low viral load compared to participants randomised to control groups after three months (Chiou et al., 2006a).

Unscheduled hospital visits were evaluated in one study (Chiou et al., 2004). In this study; two intervention groups reported statistically significant differences in pre-test and post-test scores indicating the intervention programme decreased unscheduled hospital visits, but there were no significant differences in pre-test and post-test in the control group (Chiou et al., 2004) after three months of follow-up assessments.

In the following section, I report the findings of qualitative data extracted from randomised controlled trials included in the current review. Qualitative studies of pain education studies not included in the current review were not extracted. The data explores patient's experiences and views of being part of the study as well as patient's suggestions during the development phase of the intervention.

4.12 Qualitative data within trials reviewed

Medical Research Council (MRC) (Craig et al., 2008) guidelines for development and evaluation of complex interventions recommends that qualitative interviews should be conducted to elicit views of the patients and their caregivers on the content and components of the intervention. Qualitative interviews may also be conducted after the intervention has been delivered to complement quantitative data and to get participants experiences about the intervention. Although the review did not include qualitative studies,

qualitative data embedded within educational interventional studies included in the review were extracted in order to elicit participant's experiences about the intervention.

Two studies in the current review conducted qualitative interviews after completing follow-up assessments (Webel, 2010; Gifford., et al 1998).

In the study by Webel (2010), participants reported both positive and negative comments which can be summarised into three main themes

- The intervention taught participants how to manage symptoms
- The intervention facilitated a strong sense of community
- Feeling that the facilitators could be better

Participants also added that other topics could be added to the intervention such as discordant couples and relationships, substance abuse, menopause, co-morbidities, and stress management. However Webel (2010) has not reported how participants were selected for qualitative interviews and how many were selected.

One trial conducted structured, open-ended telephone interviews (Gifford et al., 1998) which were published a year later (Gifford and Sengupta, 1999) with participants who participated in a "positive self- management programme" (PSMP) during evaluation of the programme. Responses to the programme were generally favourable, emphasizing the importance of the contracting process, group social support and the resource book which was

provided to the participants. Participants also described variation in HIV knowledge and experiences, and emphasized the importance of changes in health-related attitudes and behaviours as a result of education programme. These responses suggest that a self-management approach to HIV patient education was accepted, and could become a useful health education technique in patients with chronic HIV infection (Gifford and Sengupta, 1999).

One study conducted semi-structured interviews to elicit views from the patients and caregivers before the intervention (Gifford et al., 1998). Semi-structured, in-depth interviews were conducted among eight patients and their caregivers to identify problems they were experiencing living with HIV/AIDS, which have psychological, social and medical impacts on their quality of life. Participants raised a number of problems such as difficulties in managing symptoms, poor communication with care providers and hence depression and fatigue. Based on these problems an education programme "positive self-management programme" (PSMP) was designed and developed by physicians, nurses, health educators, community leaders (Gifford et al., 1998).

In summary, only two studies included in the current review conducted qualitative interviews. One study (Gifford et al, 1998) conducted semi-structured qualitative interviews during the development phase of the trial to elicit patients and carers needs. The same authors (Gifford et al, 1998) also conducted structured open-ended interviews to explore patient's experiences of being part of the trial. The other study (Webel, 2010) only conducted qualitative interviews after follow-up assessments to explore patient's views about the intervention.

4.13 Gaps in literature

The review of literature I have conducted has found inconclusive results on effectiveness of education interventions among people living with HIV/AIDS. Of all the eight studies reviewed one study evaluated pain as an outcome (Gifford et al, 1998). The rest focused on general symptoms that are experienced by people living with HIV/AIDS such as fatigue, stress, depression. The trial conducted by (Gifford et al., 1998) did not find sufficient evidence on the effectiveness of the education intervention in reducing pain severity among people living with HIV/AIDS.

Three of the eight studies that evaluated symptom severity and intensity as an outcome (Gifford et al., 1998, Inouye et al., 2000, Wantland et al., 2008) found evidence that the education intervention was effective in reducing severity, intensity and frequency of HIV/AIDS symptoms. One study found no significant differences between the intervention and control groups on symptom severity and frequency (Webel, 2010).

Three of the eight studies reported that educational interventions were effective on improving the quality of life of the patients (Chiou et al., 2006a, Lechner et al., 2003, Inouye et al., 2000) while two of the nine (Goujard et al., 2003, Webel, 2010) found no significant differences on the effects of educational interventions between the pain education and the usual care groups on quality of life.

Knowledge levels were reported to have improved among the participants who received the education intervention (Goujard et al., 2003, Chiou et al., 2004) while (Gifford et al., 1998) reported improved levels of knowledge among participants randomised to the control group.

Likewise (Wantland et al., 2008) reported improved self-esteem among the participants who received the self-symptom management intervention compared to the control group which received the nutrition management manual; on the contrary (Chiou et al., 2004) found no significant difference between the education intervention group and control group. Broadly the studies reported that the education intervention has no therapeutic effect that is the levels of CD4, CD8 and viral load did not differ between the intervention and control groups.

The results of the current review are not only conflicting, but also inconclusive. There are a number of reasons why the results cannot be generalised to a wider context. Firstly these studies were conducted exclusively (Gifford et al., 1998, Inouye et al., 2000, Chiou et al., 2004, Chiou et al., 2006a, Lechner et al., 2003, Goujard et al., 2003, Webel, 2010) or predominantly (Wantland et al., 2008) in western countries, where culture, delivery of services, geographical factors are very different with other countries in SSA. Although (Wantland et al., 2008) recruited participants in the USA, Puerto and South Africa, the majority of trial centres were in the USA, with small number of trial centres in South Africa.

Secondly the interventions administered in two of the eight studies I reviewed were symptom and nutritional management manuals (Wantland et al., 2008, Webel, 2010) and may not be acceptable in Malawi context. Likewise other interventions which required participants to attend training twice a week, for seven weeks (Inouye et al., 2000), weekly training for three weeks (Chiou et al., 2004, Chiou et al., 2006a), two hours weekly attendance for 10 weeks (Lechner et al., 2003), and two hour sessions for seven weeks (Gifford et al., 1998, Webel, 2010) may not be feasible, acceptable and applicable in settings like Malawi where participants have a walk long distances such as 30 km to access health care. However the important thing I noted is that the interventions did not focus much on the use of technology such as DVDs, videotapes except (Lechner et al., 2003) who used a videotape. These may not be always available in resource poor countries like Malawi and where available sustainability may be a challenge.

None of the authors in any of these eight studies reviewed included family carers as participants in their studies, although (Gifford et al., 1998) invited family carers to accompany their patients, none of them was actively involved as a participant in their study. Family carers are important in the provision of pain and symptom management for people living with HIV/AIDS in Malawi who are living in their own homes.

In summary, the review of educational interventions among HIV/ADS patients is inconclusive because the studies reviewed have produced conflicting findings. Only three of the eight studies reviewed were rated as 'good' in terms of their methodological quality, the rest were considered

methodologically poor or not possible to evaluate because of lack of methodological detail. Only one study assessed pain as an outcome and found no evidence of a positive effect. It is these conclusions that informed the design and outcomes of the pain education intervention study among HIV/AIDS patients and their family carers that is the basis of this thesis.

The next chapter reviews literature on supportive interventions targeted at family carers of people living with HIV/AIDS.

CHAPTER FIVE: REVIEW OF EVIDENCE OF THE EFFECTIVENESS OF EDUCATION INTERVENTIONS FOR CAREGIVERS OF PEOPLE LIVING WITH HIV/AIDS

5.1 Introduction

This chapter provides a detailed review of literature of published studies on the effects of education interventions for caregivers of people living with HIV/AIDS. Because carers' needs and challenges are different to patients, interventions for caregivers' interventions are reviewed separately. The chapter contains the process of conducting the review, inclusion and exclusion criteria for the studies, quality assessment of studies. In addition, the presentation of findings from the review, and gaps in literature. Although there is evidence that psychosocial and psycho-educational interventions have positive effects among family carers of people with chronic illnesses (Hudson et al., 2010) little is known about their effectiveness among carers of people living with HIV/AIDS in sub-Saharan Africa. This review critically appraises available evidence reported in randomised controlled trials and quasi experiment studies.

Systematic reviews of family carer interventions have been conducted exclusively in the UK and other countries in Europe (Victor, 2009, Stoltz et al., 2004), Australia (Hudson et al., 2010). The studies included in these reviews were for patients with cancer, schizophrenia, dementia, head injury, stroke and aphasia. Even though the needs and experiences of carers of patients with

chronic and palliative care may be similar, geographical factors may have an effect on family carers from other parts of the world, such as SSA where the prevalence of HIV/AIDS is very high. The review also aimed to critically evaluate the methodological quality of the studies.

5.2 Aims and objectives of the review

The aim of this review was to examine and update the synthesised evidence regarding the effect of pain education interventions on a range of family carer outcomes. The review sought to specify the contents and form of existing pain education interventions for family carers.

5.3 Objectives

The objectives of the review were to:

- Identify studies of education interventions for caregivers of people living with HIV/AIDS.
- Identify the educational interventional strategies used.
- Identify caregiver knowledge, self-esteem, motivation, and quality of life outcomes.

5.4 Search strategy

A comprehensive search strategy was developed and utilised to identify relevant studies published in English language only. The following data bases were searched: Amed, Assian, CINAHL, Cochrane Library, EMBASE, MEDLINE, PsycINFO and Web of Science from inception to February 2014. The following key words or subject headings were used: HIV, AIDS, carers, informal carers, family carers, education (Table 9).

All articles were screened and duplicates were deleted. Hand searching was also used by going through the reference list of articles of the identified studies that investigated the effect of education interventions on caregivers of people living with HIV/AIDS.

Table 9 Search terms used

Key concepts	**Key words**
HIV	HIV, human immune deficiency virus
AIDS	AIDS, Acquired immune deficiency syndrome
Education	carer education, carer teach, carer learn, carer inform, knowledge
Carers	Family carers, informal carers, caregivers,
Research methodology	Randomised controlled trial quasi experiment

5.5 Inclusion and Exclusion criteria

5.5.1 Inclusion criteria

Studies were included if they were:

- Randomised controlled trials, Non-randomised controlled trials or quasi

experiment studies.

- Educational interventions of any form.
- Comparison of educational intervention with usual care/standard care. Studies that looked at psycho-educational and psychosocial interventions were all included.
- Both HIV positive and HIV negative carers were included as long as they cared for people living with HIV/AIDS.
- Both caregivers and care recipients as participants.
- Qualitative data from interventional studies included in the current review will be extracted.

5.5.2 Exclusion criteria

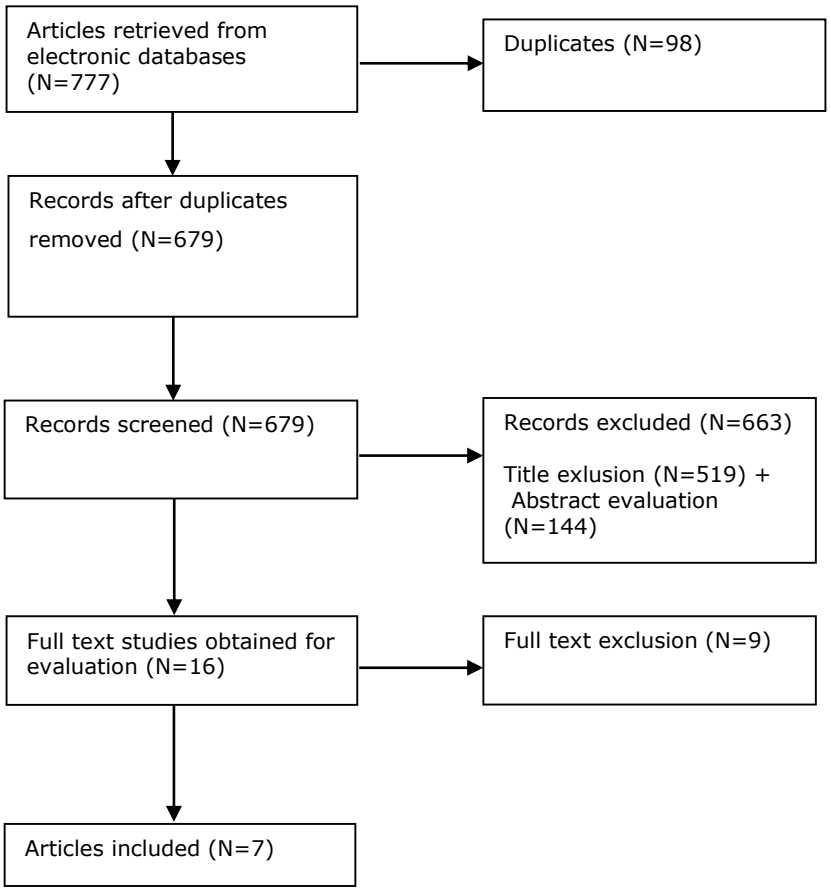
Studies were excluded if:

- Participants were paid carers such as nurses and other health care workers.
- Participants were not carers of people living with HIV/AIDS.

Table 10 Summary of Inclusion and Exclusion criteria

	Inclusion	**Exclusion**
Type of participants	Caregivers of patients with HIV/AIDS Family carers, informal carers, or any carer providing unpaid care to patients with HIV/AIDS.	Paid carers like nurses, doctors or any health care workers doing paid work, Carers of patients with other illnesses other than HIV/AIDS.
Type of studies	Randomised controlled trials, Non RCT (Quasi experiments)	Quantitative studies with different design other than RCT or quasi experiment Qualitative study only
Type of intervention	Any Educational interventions of any form like leaflet, booklet, DVD, tape recording. Psycho-educational and psychosocial interventions.	
Outcomes	Carer knowledge, QOL, positive caregivers experiences, self-esteem, anxiety, depression , stress	Any other outcomes other than the outcomes stated above.

Figure 8 Flow Diagram of the study selection process



5.6 Studies identified

The full texts of 777 papers were obtained from electronic data bases through a comprehensive and hand search. All articles were discarded if they were duplicates (N=98) and after reviewing the title of the articles (N=519). Abstracts were then reviewed and other studies were also excluded (N=144) because they did not meet the inclusion criteria (figure 8). Consequently the final articles which meet the inclusion criteria were obtained for evaluation (N=16). After full text extraction nine studies were excluded because they were not intervention studies, or the intervention was cognitive-behavioural therapy and were caregivers of mental retardation patients, though received intervention on HIV/AIDS information. Summary of all studies included in the review are presented in table 12.

All the seven studies included in the review were critically evaluated on a checklist recommended by the Centre for Review and Dissemination (Centre for Review and Dissemination, 2009) and Critical Appraisal Skills Programme (Critical Appraisal Skills Programme, 2013) for evaluating randomised controlled trials as explained in chapter four.

Participants in all the studies were not blind to group allocation. Given the nature of the interventions, blinding was not feasible. The sample size ranged from 28 (Gordon-Garofalo and Rubin, 2004) to 307 (Rotheram-Borus et al., 2001) participants. Three of the seven studies in this review were randomised controlled trials and random allocation was performed effectively (Hansell et al., 1999, Rotheram-Borus et al., 2001, Pakenham et al., 2002). Four of the

seven studies were quasi experiment (Pomeroy et al., 1995, Boon et al., 2009b, Smith Fawzi et al., 2012, Gordon-Garofalo and Rubin, 2004). Two of the four quasi experiment studies had a control group (Pomeroy et al., 1995, Gordon-Garofalo and Rubin, 2004). Two of the seven studies (Pakenham et al., 2002, Boon et al., 2009b) reported that outcome assessors were blind to group allocation and two of the seven studies reported that participants self-completed the questionnaires (Hansell et al., 1999, Pomeroy et al., 1995). Only one of the four randomised controlled trails reported that outcome assessors were not blind (Smith Fawzi et al., 2012), however (Rotheram-Borus et al., 2001, Gordon-Garofalo and Rubin, 2004) did not report who conducted outcomes and whether they were blind or not.

Of the five studies which had a control group, participants were broadly similar at baseline, except age (Hansell et al., 1999), sex and occupation (Pomeroy et al., 1995) differences. All the seven studies achieved 80% follow-up except (Hansell et al., 1999) who reported 44.2% attrition. One study (Rotheram-Borus et al., 2001) did not clearly state how many participants were lost to follow-up, although they report that follow-up rate was 'very good'. Three studies stated how data analysis was conducted; one performed intention-to-treat analysis (Rotheram-Borus et al., 2001), modified intention-to-treat analysis (Pakenham et al., 2002) and per protocol analysis (Boon et al., 2009b). All studies provided information about characteristics and reasons for lost to follow-up. The main reasons were death of the patient, death of the caregiver, or carers work commitments.

Table 11 Quality assessment of the RCTs included in the review

Studies	Random allocation	Blinding of participants	Analysis of withdrawal	Blinding of assessor	Groups comparable at baseline	Identical except intervention	Complete follow up	Overall quality
Hansell et al (1999)	Yes	No	No	Self-completed by participants	Seronegative caregivers were older than seropositive caregivers	Yes	No	3/7
Rotheram-Borus et al (2001)	Yes	No	ITTA	Not stated	Yes	Yes	Yes	4/7
Pakenham et al (2002)	Yes	No	Modified ITTA.	Yes, some were self-completed by participants	Yes	Yes	Yes, 80% completed follow-up	4/7
Gordon-Garofalo and Rubin (2004)	No	No	Yes	Not stated	More homosexuals and bisexual partners in the intervention group More participants in treatment compared to control group	Yes	Yes	3/7
Pomeroy et al (1995)	No	No	No	Self-completed by participants	Sex and occupation differences	Yes	82% completed follow-up	3/7
Fawzi et al (2012)	No	No	No	No	N/A	N/A	Yes	1/7
Boon et al (2009)	No	No	Per protocol analysis.	Yes	N/A	N/A	Yes, 90% completed follow-up	2/7

All the seven studies included in the review were considered of 'poor' quality. None of the seven studies scored above four out of seven (a 60% cut-off point). The methodology was either poorly described or not clearly stated.

5.7 Nature of Interventions

The interventions tested have been summarised in table 12. Broadly speaking the nature of the interventions were similar. They were psychosocial (Smith Fawzi et al., 2012, Pakenham et al., 2002) and psycho-educational (Boon et al., 2009b, Rotheram-Borus et al., 2001, Hansell et al., 1999, Pomeroy et al., 1995) interventions delivered to family caregivers of patients infected with HIV/AIDS. The caregivers were either blood relations or foster parents or extended family members or partners/spouses for the people living with HIV/AIDS. The interventions were delivered by social workers (Pomeroy et al., 1995, Rotheram-Borus et al., 2001, Smith Fawzi et al., 2012, Hansell et al., 1999), community health workers (Boon et al., 2009b) and clinical psychologists (Pakenham et al., 2002). All interventions were group based. Three of the seven studies (Hansell et al., 1999, Rotheram-Borus et al., 2001, Pakenham et al., 2002) were randomised controlled trials and had two parallel groups, the intervention and usual care groups, except (Pakenham et al., 2002) had three parallel groups. In the first intervention group the intervention was delivered to both caregivers and care recipients (carer/patient dyads), in the second intervention group the intervention was delivered to caregivers only) and in the third group both caregivers and care recipients received usual care, but received the intervention after completing follow-up assessments (wait list control).

In these three randomised controlled trials, the interventions were social support boosting to reduce experience of stress and enhance coping. Participants randomised to the intervention arm received network resources,

specific supportive behaviour. The intervention was delivered monthly for 12 months. Participants randomised to the control group received usual care consisting of multidisciplinary team approach and access to medical and nursing care (Hansell et al., 1999). The intervention in another study was eight weekly sessions, each session lasting one and half hours on psychological counselling on emotional problems, social problems, and dealing with health/infection concerns and caregiving demands (Pakenham et al., 2002). All sessions were conducted by clinical psychologists. In another randomised controlled trial, participants randomised to the intervention group were taught coping skills with HIV/AIDS illness, fear, anger, caregiving responsibilities and how to provide care, while the control group received standard care. The intervention was delivered by social workers and participants attended educational sessions each Saturday. The sessions lasted four hours (two hours in the morning, and two hours in the afternoon). In total they attended eight sessions (Rotheram-Borus et al., 2001).

In quasi experimental studies participants allocated to the intervention group were taught basic facts about HIV/AIDS, stigma coping skills, management of opportunistic infections, management of anger, stress and anxiety, and to be assertive. The control group received usual care (no details provided), but received the intervention after follow-up assessments were completed. Participants attended eight sessions delivered weekly in groups of 8-10. Each session lasted 90 minutes (Pomeroy et al., 1995). In another study, a similar intervention as described above was delivered to partners and spouses of people living with HIV/AIDS. The control group received routine social services

such as peer support, and family counselling and were invited to receive the intervention after completing follow-up assessments (Gordon-Garofalo and Rubin, 2004).

In another quasi experimental study (Boon et al., 2009b) older caregivers attended four workshop sessions delivered monthly each lasting three hours on basic information about HIV/AIDS, home-based and nursing care, social assistance and support. Participants received the intervention in groups of 10-12, but there was no control group (Boon et al., 2009b).

In their study (Smith Fawzi et al., 2012) participants were taught coping skills and social support enhancement, positive living, stress reduction strategies, HIV risk behaviour reduction. Participants received the intervention in groups of 12-15 bi-monthly over a year and there was no control group (Smith Fawzi et al., 2012).

Three of the seven studies (Pomeroy et al., 1995, Pakenham et al., 2002, Gordon-Garofalo and Rubin, 2004) invited participants in the control group to receive the intervention after completion of follow-up assessments. The use of educational materials were not common in the studies reviewed except (Pomeroy et al., 1995, Boon et al., 2009b) who provided hand outs to study participants.

Table 12 Summary of interventional studies included in the review

Author/Setting	Sample	Intervention(s)	Comparator	Outcomes/measurers	Results
Hansell, et al (1999); New York/New Jersey	70 primary caregivers of children with HIV/AIDS	Social support consisting of support network resources, supportive behaviour, and subjective appraisal of support facilitated by social workers	Standard care consisting of multidisciplinary team approach, medical and nursing care, social and respite care	1.Total caregiver stress measured with The Derogatis Stress Profile (DSP) 2.Interpersonal relationships measured with The Tilden Interpersonal Relationship Inventory (TILDEN) 3. Internal and external family coping measured with The Family Crisis Oriented Personal Scales (F-COPES) 4. Social status evaluated with Hollingshead Index of Social Position. All outcomes were conducted at 0,6,12 months	1-4. No significant differences were found between intervention and control groups at 6 months in all the four outcomes. 4. When adjusted for HIV status of the caregivers, social support for HIV negative caregivers was significantly different compared to the sero positive caregivers between the two groups.
Pakenham et al (2002) Australia	36 caregivers and care-recipients with HIV/AIDS	Dyad intervention (DI) caregivers and their patients: eight weekly sessions of one and half hours conducted by psychologists Caregiver Intervention (CI) caregivers only: eight weekly sessions of one and half hours conducted by psychologists	Wait list control group (WLC); details of standard care not provided.	1.Global distress: The Brief Symptom Inventory (BSI) 2.Dyadic adjustment: Dyadic Adjustment Scale 3.Target problem ratings: Target problem rating scale 4.Social adjustment: The Psychosocial Adjustment to Illness Scale 5.Subjective health status: Global rating of health scale 6.Knowledge:HIV/AIDS knowledge questionnaire (at 0,2 and 4 months for all six)	1-3.Caregivers in the DI group improved significantly compared to CI and WLC on (global adjustment, dyadic adjustment and target problem) which were maintained at four months except global distress 2-6. Care recipients in the DI group improved significantly in all outcomes compared to care recipients in the CI and WLC which were maintained at four months except knowledge

Author/Setting	Sample	Intervention(s)	Comparator	Outcomes/measurers	Results
Boon et al, (2009) Port Elizabeth in South Africa	202 older caregivers of orphaned and sick children with HIV/AIDS	Four weekly workshop sessions, each for three hours consisting of information about HIV/AIDS, communication, skills about home-based and nursing care, social assistance and social support. Training was facilitated by community health workers in groups of 10-12 older carers	No control group	1. perceived ability to provide care 8-item questionnaire 2.Knowledge on HIV/AIDS 10-item questionnaire 3.Depression was measured with Hopkins Symptom Checklist-25 item questionnaire 4. Coping measures was assessed with Ways of Coping Checklist. All outcomes were conducted at baseline, after intervention and three months follow-up	Of the 202 participants, 141 attended all the sessions, 13 did not attend all the four and 48 did not attend any sessions. 1. Participants who attended the workshop perceived themselves to more able to provide nursing care (P<0.003) compared to participants who did not attend 2. Improved knowledge on HIV/AIDS (p<0.003) than those who did not attend 4.Caregivers showed higher coping skills at post-test and follow-up
Fawzi et al (2012) Haiti	168 HIV affected youths and 130 caregivers	Enhancing coping skills and increasing social support sessions held bi-monthly for one year. Groups of 12-15 participants (parent-child pairs) facilitated by social workers	No control group	1.Severity of depression symptoms: Hopkins Symptom Checklist (HSCL-25) 2.Social support: to examine confidence, network size and instrumental support 3.HIV-related stigma: HIV-related stigma questionnaire 4.Level of role functioning: ACTG Short Form-21 (SF-21) Outcomes were conducted at baseline and one year after the intervention	1-3.Caregivers demonstrated significant reduction in depressive symptoms, improved social support and decreased HIV-related stigma

Author/Setting	Sample	Intervention(s)	Comparator	Outcomes/measurers	Results
Gordon-Garofalo and Rubin (2004)	28 partners and spouses of people living with HIV/AIDS	Psychoeducation intervention on the following areas: general information about HIV/AIDS, Infections associated with HIV/AIDS, positive, coping, dealing with anger, stress, and stigma. The intervention was delivered weekly for eight weeks, each session lasting 90 minutes.	Waiting list control received routine social services such as peer support, and family counselling	1.Depression was measured with 21-item Beck Depression Inventory (BDI) 2. Anxiety was assessed with the State-Trait Anxiety Inventory (STAI), A 20-item questionnaire. 3. Perceived social support was assessed with the Social Support Appraisals (SSA) 4.Percieved stress was assessed with a 15-item measure The Impact of Event Scale (IES) 5. Perceived stigma was assessed with a 3-item questionnaire developed Pomeroy et l (1995). All outcomes were conducted at 0 and 2 months.	1-5.No significant differences between two groups in all the five outcomes. 1-3. The treatment group mean showed a better improvement compared to the control group.

Author/Setting	Sample	Intervention(s)	Comparator	Outcomes/measurers	Results
Pomeroy (1995) south-western metropolitan area	33 family carers	Eight sessions delivered weekly to family caregivers in groups of 8-10. The sessions covered topics such as basic facts about HIV/AIDS; coping with stigma, management of opportunistic infections, anger management, stress management, assertiveness, anxiety management, and nutrition in HIV/AIDS. Each sessions lasted 90 minutes.	Waiting list control received standard care	1.Depression: The Beck depression inventory (BDI) was used to assess depression 2.Stigma: 3-item questionnaire 3.Perceived stress: The impact of event (IES) was used to measure stress 4.Anxiety: Trait Anxiety Inventory (STAI) 5.Social support: The health and daily living form (HDL) assessed social support (all assessed at 0,2,4 months)	1-4. Results were statistically significant for stress, stigma, depression and anxiety (P<0.001) at 2 and 4 months.
Rotheram-Borus et al (2001) New York in the USA	307 parents and 412 adolescent children with HIV/AIDS (153 parents and 205 youth in the intervention; 154 parents and 207 youth in the control group)	Two modules: first modules to parents alone (four Saturdays); Second module: both parents and adolescents (eight Saturdays). Sessions lasted 2 hours in the morning and 2 hours in the afternoon; with group meetings of 8-10 parents or adolescents separately. Topics mainly focused on coping with illness and caring for children.	Standard care	1.Symptoms of emotional distress: Brief Symptom Inventory (BSI-53) 2.Coping: Five Coping with Illness Questionnaire Outcomes were conducted at three months interval over 24 months	1.Significant reduction in emotional distress over 3-15 months

5.8 Outcome measurers

Each study included had a variety of outcomes. Broadly the outcomes measured in the studies were anxiety, depression, stress, coping, social support and HIV/AIDS knowledge.

In the three randomised controlled trials, the outcomes were total caregiver stress measured with the Derogatis stress profile (DSP); interpersonal relationships measured with the Tilden Interpersonal relationship Inventory (TILDEN); family coping measured with The family Crisis Oriented Personal Scale (F-COPES) and social status measured with Hollingshead Index of social position. All outcomes were conducted at 0, 6 and 12 months (Hansell et al., 1999). The trial reported that there were no significant differences between the intervention and control groups in all the outcomes, although caregivers who were HIV positive had significant greater stress levels and used fewer coping strategies compared to caregivers who were HIV negative (Hansell et al., 1999). The trial had high attrition rate, only (n=39) of the (n=70) caregivers who were recruited remained in the study at 12 months and due to small sample size, there was no sufficient power to conduct the analysis at 12 months of follow-up assessment. In another randomised controlled trial (Rotheram-Borus et al., 2001) caregivers were assessed for symptoms of emotional distress and anxiety with Brief Symptom Inventory (BSI-53), coping with illness was assessed with a five-item coping with illness questionnaire, an index of adult problem behaviours was used to evaluated presence of risk behaviour such as substance use, degree of distress was evaluated by a distress 1-5 Likert scale. The authors reported that caregivers who were

randomised to the intervention group experienced significant decrease in depression, anxiety, problem behaviours and distress compared to caregivers who were randomised to the control group over 3 to 15 months. The changes were not significant after 18 to 24 months except for the problem behaviour outcome (Rotheram-Borus et al., 2001). The other randomised controlled trial (Pakenham et al., 2002), evaluated caregivers in terms of Global distress using The Brief Symptom Inventory (BSI), social adjustment using the Psychosocial Adjustment to illness Scale, dyadic adjustment using the Dyadic Adjustment Scale, health status using the Global Rating of health Scale, problem rating using the Target Problem Rating Scale and knowledge using the HIV/AIDS knowledge questionnaire. All outcomes were evaluated at 0, 2 and 4 months. This is the only trial which had three parallel groups. The authors reported that both intervention groups (caregivers with their care recipients and caregivers only) showed a greater improvement in all the outcomes except social adjustment. Care recipients who received the intervention with their caregivers showed greater improvement on global distress, dyadic adjustment, target problems than care recipients who did not receive the intervention (Pakenham et al., 2002).

Table 13 Outcomes of interventions among caregivers of people living with HIV/AIDS

Studies / Outcomes	Hansell et all (1999) (n=70)	Rotheram-Borus et al (2001) (n=307)	Pakenham et al (2002) (n=36)	Pomeroy et al (1995) (n=33)	Fawzi et al (2012) (n=130)	Boon et al (2009) (n=202)	Gordon-Garofalo and Rubin (2004) (n=28)
Psychological							
Depression		↓		↓	↓		=
Stress	=			↓			=
Anxiety		↓		↓			=
Distress		↓	↓				
Coping	=					↑	
Social							
Stigma				↓	↓	↓	=
Social support	=			=	↑		=
Social adjustment			=				
Dyadic adjustment			↑				
Knowledge			↑			↑	

=: No difference

↓: Significant decrease in the intervention group

↑: Significant increase in the intervention group

In the four quasi experimental studies (Pomeroy et al., 1995, Boon et al., 2009b, Smith Fawzi et al., 2012, Gordon-Garofalo and Rubin, 2004) most outcomes evaluated were similar such as depression, social support and coping. However they all used different tools to evaluate outcomes, and broadly the results were similar.

In the study Pomeroy et al (1995) evaluated depression with The Beck depression inventory (BDI), stigma was evaluated by a questionnaire developed by the researchers, perceived stress was measured with the impact of event (IES), anxiety was measured with trait anxiety inventory (STA1), and social support was assessed with the health and daily living form (HDL). All outcomes were conducted at 0, 2 and 4 months. The study reported statistically significant findings among participants in the intervention group compared to participants in the control group for all outcomes (stress, stigma, depression, anxiety), expect social support (Pomeroy et al., 1995).

In another study among partners and spouses of people living with HIV/AIDS Depression was measured with 21-item Beck Depression Inventory (BDI), anxiety was assessed with the State-Trait Anxiety Inventory (STAI), a 20-item questionnaire, perceived social support was assessed with the Social Support Appraisals (SSA), perceived stress was assessed with a 15-item measure. The Impact of Event Scale (IES) and perceived stigma was assessed with a 3-item questionnaire developed Pomeroy et al (1995) as above. All outcomes were conducted at baseline and eight weeks after the intervention. In this study, the authors reported that there were no significant differences between the partners and spouses who received the intervention and those who did not receive the intervention, even though the treatment group mean showed a better improvement compared to the control group in depression, anxiety and social support (Gordon-Garofalo and Rubin, 2004).

In another study (Boon et al., 2009b) assessed depression with Hopkins Symptom checklist, coping measurers was evaluated with ways of coping

checklist. All outcomes were conducted at baseline and three months after delivery of the intervention. This study did not have a control group. The authors reported that participants who attended the workshop sessions perceived themselves to be more able to provide care, perceived more control over nursing care activities, had more positive attitudes towards people living with HIV/AIDS and showed improved knowledge (Boon et al., 2009b). The results were statistically significant when compared with participants who did not attend either all or none of the sessions.

Another study Smith Fawzi et al (2012) evaluated depression sub-scale from the Hopkins symptom check list (HSC-25), social support assessment to examine having a confidant, network size, and level of instrument support, role functioning of parents/caregivers evaluated with ACTG short form-21 (SF-21) and HIV-related stigma was evaluated with the HIV stigma questionnaire. All outcomes were conducted at baseline and a year after the intervention. It was reported that caregivers (95%) who were HIV positive themselves demonstrated statistical significant reduction in depressive symptoms, decreased HIV-related stigma and improved social support, however there was no control group in this study (Smith Fawzi et al., 2012).

In the following section a description of the findings of qualitative data extracted from the interventional studies included in the current review is provided. The findings include data gathered during the development phase of the intervention, and data gathered after carers participated in the intervention.

5.9 Qualitative data within studies reviewed

The use of qualitative data was not common in the studies reviewed. Only one study Smith Fawzi et al (2012) conducted focus group after the intervention to elicit caregivers experiences of being part of the study. Social workers held focus group discussions to compile information on participants' impressions of the sessions, suggestions for improvement, and what they learned from the sessions. Individual interviews were also conducted with five caregivers from the six study sites. As reported earlier the study was a psychosocial support intervention on enhancement of coping skills and increasing social support. Participants were evaluated for depressive symptoms, stigma and social support. The quantitative data reported that participants demonstrated significant decrease in depression, HIV-related stigma and improved social support. The qualitative data supported these findings and two main themes emerged from the data:

- Renewed sense of hope after the intervention
- Another participant expressed that they learned how to cope after attending the group sessions
- Greater confidence in coping with HIV-related stigma

Findings from the qualitative interviews have supported the quantitative data on the improvement in coping with HIV/AIDS illness, reduced depressive symptoms and positive attitude on HIV-related stigma, although the authors

did not report how the participants were selected for individual qualitative interviews.

Three studies held qualitative interviews before the delivery and implementation of the intervention (Smith Fawzi et al., 2012, Boon et al., 2009b, Rotheram-Borus et al., 2001). There was use of focus groups and qualitative interviews among caregivers to develop the curriculum, this was facilitated by social workers and psychologists, and through this adaptations were made before the intervention was delivered. Initially the curriculum was designed to hold group sessions weekly for six month, but it was changed to bi-monthly sessions over one year (Smith Fawzi et al., 2012). However it is not clear if the caregivers were also asked to give input on the content of the intervention.

The study conducted by Boon et al (2009) recruited older caregivers aged 60 years and above. To design and develop the intervention focus group discussions were conducted among community health workers of Age-in-Action and interviews were conducted with senior staff of Age-in-Action for possible topics and contents to be included. The development of the intervention was based on a quantitative survey among older caregivers of people living with HIV/AIDS (Boon et al., 2009a). Likewise Rotheram-Borus et al, (2001), conducted qualitative study and piloted the intervention before the implementation of the intervention, and was designed based on the previous experiences of people living with HIV/AIDS.

In summary qualitative interviews were conducted only in one study (Smith Fawzi et al, 2012) to elicit views ans experiences from carers about the intervention on completion of follow-up assessments. Three studies conducted qualitative interviews and focus groups during the development phase of the intervention (Smith Fawzi et al., 2012, Boon et al., 2009b, Rotheram-Borus et al., 2001).

5.10 Gaps in literature

The studies reviewed have reported that psychosocial and psycho-educational interventions are effective in reducing depression, anxiety, stigma, distress, stress and improving social support and knowledge among caregivers of people living with HIV/AIDS. Only one study (Hansell et al., 1999) found no difference on stress levels, coping skills and social support among caregivers randomised to intervention and control groups. This study had a small sample size (n=70) and many participants were lost to follow-up (n=31) due to death and work commitments and illnesses of both caregivers and patients. Only one study; (Pakenham et al., 2002) had caregiver patient dyad group which was compared with caregiver only group and wait-list control group. Although the study reported significant findings for distress reduction, knowledge improvements and dyadic adjustments, there was no difference on social adjustment between the caregiver and care recipient/patient group compared with the caregiver only or wait-list control group. The study had a small sample size (n=36) caregivers randomised to two treatment and one wait-list

control groups. The only randomised controlled trial (Rotheram-Borus et al., 2001) with a larger number of study participants (n=307) and low attrition rate, reported significant findings for depression, anxiety and distress among participants randomised to the intervention group compared to participants randomised to the control group.

The rest were not randomised controlled trials (Pomeroy et al., 1995, Boon et al., 2009b, Smith Fawzi et al., 2012) and did not have a control group (Boon et al., 2009b, Smith Fawzi et al., 2012). However all the three studies reported significant findings on reducing stigma (Pomeroy et al., 1995, Boon et al., 2009b, Smith Fawzi et al., 2012), decreased depression (Smith Fawzi et al., 2012, Pomeroy et al., 1995) , stress and anxiety (Pomeroy et al., 1995), improved coping and knowledge (Boon et al., 2009b).

These studies were predominantly conducted in western countries, except (Boon et al., 2009b) was conducted in South Africa. The interventions were mainly psychosocial and psycho-educational with particular focus on psychological outcomes. No study was found with specific focus on education interventions on pain among caregivers of people living with HIV/AIDS, suggesting there is not much research conducted on this subject. Only one study; Boon et al., (2009) conducted outcomes on caregiver motivation to provide care, perception to provide care, and ability to provide care to their loved ones.

The methodological quality of the studies included in both systematic reviews was poor. Only three of the eight studies of educational interventions among

HIV/AIDS patients and none of the seven studies of family carers had a methodological quality score of five or more out of seven. Only two studies included in the review of educational interventions among family carers were randomised controlled trials. The rest were either non-randomised or did not include a control group. The results of the two systematic reviews were therefore inconclusive. On this basis I designed a pain education intervention to be used by people with HIV/AIDS and their family carers that was formally tested using a randomised controlled trial.

The next chapter therefore contains a detailed discussion of the methodology and methods of conducting the randomised controlled trial for pain education intervention on which the current study is based on.

CHAPTER SIX: METHODOLOGY

6.1 Introduction

This chapter describes the methodological approach and methods of data collection employed in this study. This study was a randomised controlled trial (RCT) to test the effectiveness of an educational intervention comprising of an information leaflet, face-to-face verbal instruction and phone call reminder after two weeks following the delivery of the intervention. Effectiveness was judged in terms of reducing pain, improving knowledge, improving quality of life and improving motivation among people living with HIV/AIDS and their family carers at two public hospitals in Malawi.

This chapter looks at the design of the study, the eligibility criteria for entry into the study, the process of identification of study participants, the process of recruitment and the process of obtaining and gaining informed consent from participants. In this chapter I describe the process of recording baseline measures, the process of randomisation and the components of the intervention and usual care that constituted the two treatment arms in the trial. It also includes a discussion on how the follow-up assessments were conducted. In this chapter I also describe the outcomes of interest and tools used to measure these outcomes. The ethical considerations relating to the decisions made about the design and to the implementation of the study are also explored.

6.2 Study Design

A randomised controlled trial is a methodology in which participants are allocated to either treatment or control groups at random (Stolberg et al., 2004). A randomised controlled trial is the gold standard for evaluating the effectiveness of an intervention because of its scientific rigour (Lewith and Little, 2007, Akobeng, 2005a). Randomised controlled trials provide the best evidence for effectiveness of interventions (Stolberg et al., 2004). Random allocation is the assigning of participants into either intervention or control groups at random (Sibbald and Roland, 1998, Stolberg et al., 2004), in order to minimise selection bias, allocation bias and systematic bias (Pocock, 1983, Roush, 2008). Selection bias refers to the selection of individuals, groups or data for analysis such that proper randomisation is not achieved, thereby ensuring that the sample obtained is not representative of the population intended to be analyzed. Allocation bias occurs during the process of allocating participants to either experiment or control groups. In this study opaque sealed envelopes were used to conceal allocation of study participants to either the pain education intervention or wait list control groups. Bias can also be systematic or performance bias, where there are systematic differences in the care provided to study participants in the comparison group other than the intervention group, this can be minimised by blinding study participants and health care providers so that they do not know about group allocation (Bulpitt, 1996). Blinding prevents participants, health care workers and researchers having knowledge that might influence/favour the results of the experiment (Schulz et al., 1995). Blinding can be double or single blinded. Double blinding is where both participants, health care workers, researchers, assessors are not

aware of group allocation (Chan, 2003). Single blinding is where either participants or investigators, or health care workers or assessors are aware about group allocation. The pain education intervention study was a single blinded study because patients, family carers and I were aware of group allocation; however outcome assessors and health care workers were not aware.

Open studies exaggerate effects of treatment by 17% (Schulz et al., 1995), however double-blind studies are not always feasible (Campbell et al., 2000). Use of placebo controls help to maximise blinding, but in complex interventions they are difficult to develop (Jadad and Enkin, 2007). However single blinding can be implemented in complex interventions where you may blind the assessor to minimise measurement bias (Jadad and Enkin, 2007, Bulpitt, 1996).

Randomisation helps to adjust for known confounders like age, sex, education and unknown confounders such as undiagnosed co-morbidity (Day and Altman, 2000, Saks and Allsop, 2007) so they are distributed equally within the groups so that the differences observed in the outcomes can only be explained by the treatment received (Jadad and Enkin, 2007, Stolberg et al., 2004). The allocation is not determined by the researcher, study participants or clinicians (Jadad, 1998). Because of this the findings generated from a randomised controlled trial are likely to be closer to the true effect of the intervention than the findings generated by other research methods (Gray and Pinson, 2003).

This pain education study was a two-centre wait list controlled trial.

Participants in each centre were randomised to either an experimental group or a control group. Those allocated to the experimental group received a leaflet-based educational intervention and face-to face verbal instructions for approximately 30 minutes on pain assessment and management in addition to usual care and follow-up phone call reminder after two-weeks. Those allocated to the control group received usual care, but received a leaflet on completion of follow-up measures for both groups (wait list control) (Polit and Beck, 2008). Randomisation does not, however protect against other forms of bias such as attrition bias (Jadad and Enkin, 2007). This can be minimised by performing intention-to-treat analysis, whereby outcomes are analysed with respect to the groups they were originally allocated to irrespective of whether they experienced the intended intervention or not (Lewith and Little, 2007). This maintains the advantage of random allocation which may be lost through withdrawal or noncompliance to treatment (Sibbald and Roland, 1998).

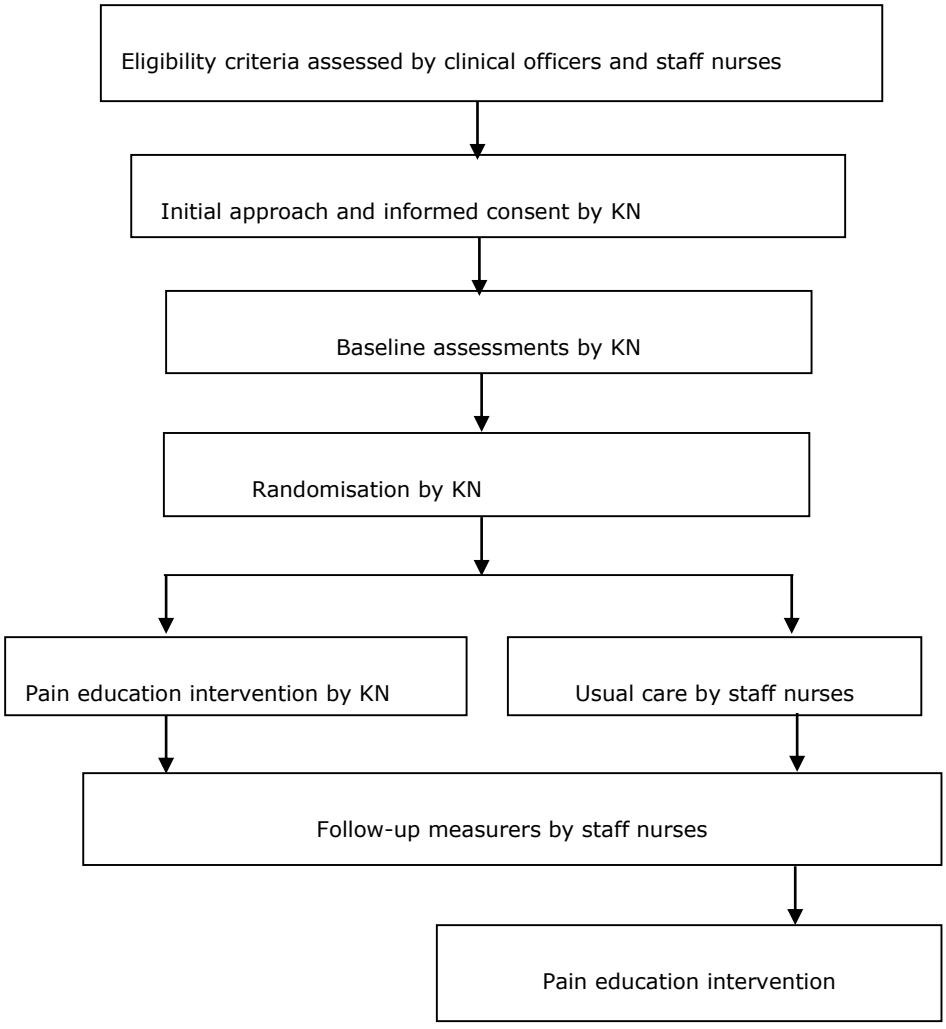
These features in a randomised controlled trial enhances reliability and validity (internal and external) of the results by preventing systematic error/bias (Moher and Olkin, 1995). Reliability refers to consistency of data obtained from a study, for instance how accurate the tool is in performing a procedure or collecting required data (Polit and Beck, 2008). Internal validity is concerned with the validity of the inferences, that is the confidence that the independent variable, rather than other factors caused a change (or not) in the outcome (Jadad and Enkin, 2007). External validity concerns the generalizability of causal inferences; this is a critical concern for randomised controlled trials as it aims to yield evidence based practice (Jadad and Enkin,

2007). Randomisation, therefore controls all threats to internal validity and reliability (Polit and Beck, 2008). However randomisation does not control all threats to external validity.

The philosophy of evidence-based practice assumes that randomised controlled trials offer stronger evidential support (Hjorland, 2011). Evidence based medicine was born on the philosophy of empiricism, which stresses that our actions and decisions should be based upon the best scientific evidence (Hjorland, 2011), using mathematical estimates of probability and risk (Samarkos, 2006). Critics argue that evidence-based medicine has inherited all the weaknesses of empiricism and there is no strong evidence that practising evidence-based medicine improves patient outcomes, practitioners autonomy is restricted and practitioners experiences and patients perceptions are afforded a low priority (Hjorland, 2011, Cartwright, 2007).

In this study the two groups were treated and observed identically except that one group received the intervention so that any differences detected in outcomes might be explained due to the intervention received (Akobeng, 2005a). The design of the pain education interventional study is illustrated in Figure 9.

Figure 9 The design of the pain education intervention study



6.3 Settings and access

The study took place in two public hospitals in the northern part of Malawi, Ekwendeni Mission Hospital and Mzuzu Central Hospital. Both Ekwendeni and Mzuzu are teaching hospitals. I obtained access to Ekwendeni Hospital by telephoning the HIV clinic co-ordinator at Ekwendeni Hospital during the design stage of the trial. This was to explain the overall aims and objectives of the study, and potential contribution from the study. Access to Mzuzu Central Hospital was obtained after the trial had already commenced. The initial plan was to conduct the study at one centre (Ekwendeni Hospital), but during the pilot phase of the study, I observed that recruitment was slow, and I thought two centres were needed to hasten recruitment as explained later in this chapter. I therefore contacted the Chief Nursing Officer at Mzuzu Central Hospital by phone and explained to him about the project. He then advised me to make a formal application to the ethical committee to review the study at Mzuzu Central Hospital. After the committee reviewed the proposal; access to conduct data collection at Mzuzu Central Hospital was granted (Appendix 12). The population served by these hospitals includes people from both rural and urban areas.

6.3.1 Ekwendeni Mission Hospital

Ekwendeni Mission Hospital is run by the Christian Health Association of Malawi (CHAM). It is about 20 km from Mzuzu City (Figure 2 in chapter two).

Ekwendeni Hospital is a general hospital and provides secondary level health services (Figure 1 in chapter two).

It has a palliative care clinic which provides palliative care services such as pain medication, counselling and psychosocial support to patients with chronic conditions like HIV/AIDS, cancer, heart problems and other long term illnesses. The palliative care clinic runs every working day and patients report with various kinds of problems for which care and support is provided depending on the needs of each patient. The palliative care clinic is run by clinicians who have basic training in palliative care.

The hospital has an HIV clinic, which was opened in 2005 where HIV medications are provided. The clinic is known as 'Wanangwa' clinic. This is Tumbuka language, a local language in Malawi which means freedom. The clinic opens on Tuesday, Wednesday and Thursday for supply of drugs to patients. Wednesday afternoon is the clinic session for the clients who are newly registered to attend a health education session before they can start treatment. Patients on HIV medication come to the clinic every month for assessment and to collect drugs. The clinic has four clinical officers and twelve nurses who provide services to patients with HIV/AIDS and their carers. HIV clinic nurses and clinicians also provide palliative care services.

6.3.2 Mzuzu Central Hospital

Mzuzu Central Hospital is a referral hospital for the whole of northern Malawi comprising of several departments, including the HIV/AIDS clinic known as "Rainbow Clinic" which was opened in 2004. This is the first HIV/AIDS clinic in the Northern Malawi. It is supported by the Malawian government. The clinic is open from Monday to Friday for all the patients, however Monday and Wednesday are special days for Paediatric and staff patients, Tuesday and Thursday are for adult patients. Like Ekwendeni Hospital, there is a palliative care clinic for all patients with chronic illnesses, and HIV/AIDS being one of them, unlike Ekwendeni Hospital, the palliative care clinic has got its own staff members. There are three palliative care nurses. The HIV clinic has five nurses and four clinical officers, even though only two are full time clinical officers based at the HIV clinic.

Pain medication is not always available, but when available may not always be prescribed by health professionals. The pain education intervention was designed, developed and delivered to inform the patients how to assess their own pain, classify it and report this to health professionals, so that when opioids are available they should be available for prescribing.

6.4 Study Participants

Participants were people living with HIV/AIDS and their family carers.

6.4.1 Inclusion criteria for PLWHA

To be eligible for the trial, participants had a diagnosis of HIV/AIDS. Participants with other conditions such as cancer and tuberculosis were included if they presented alongside a diagnosis of HIV/AIDS. Eligible participants with HIV/AIDS were at WHO clinical stages III or IV of HIV/AIDS, or with a CD4 cell count of less than 350 cells, when the presence of pain and other symptoms are more likely due to opportunistic infections or side effects of HIV treatment. Staging for trial eligibility was assessed from the medical records if recorded or through assessment by clinic staff if this information was not available in the medical records. All participants were able to read and write in English or Tumbuka (the vernacular/local language used in the northern part of Malawi). They were adults aged 18 years or over.

6.4.2 Inclusion criteria for carers

To be eligible for inclusion, carers were those living with the person with HIV/AIDS and were identified as the individual most involved in their care.

6.4.3 Exclusion criteria for people living with HIV/AIDS

People living with HIV/AIDS were excluded if they had a health problem which hindered cognition and communication such as HIV-associated dementia. This

was assessed by the attending clinical officers during history taking at the initial assessment or at clinic review.

6.5 Recruitment of participants

People living with HIV/AIDS in Malawi typically visit the hospital (Palliative care and HIV clinics) with their family members. Posters about the study entitled 'Pain Education Study' (Appendix 14) were prominently displayed and potential participants had the opportunity to be given further information about the study directly from clinic staff or myself. All participants routinely have their weight checked and recorded during every visit to the clinic before they are reviewed by a nurse or clinical officer. During this time the study was introduced to potential participants.

The study was introduced either during the first appointment at the HIV clinic for newly registered patients (figure 10a)or during routine appointments at the HIV clinics or palliative care clinics for those who are already receiving HIV medication (Figure 10b). Participants were informed about the study and were provided with an information sheet (appendix 1).

All newly registered patients attended a health education session with their family carers focussing on drug adherence. A further detail about the study was provided to the participants when necessary (these sessions were held every Tuesday and Thursday at Mzuzu central hospital and every Wednesday at Ekwendeni hospital). This was to ensure that participants understood the

salient information required for them. Participants were advised that inclusion in the study would not affect their treatment at the HIV clinics and that if they decide to participate in the study, they were free to withdraw at any time they wished. Potential participants were encouraged to discuss the study with their family members before making a decision to take part in the study. Potential participants had between two and four weeks' to consider taking part in the study.

During their next appointment, participants who were interested in taking part in the study came to me to express their interest. Participants were asked if they understood what the study is all about and if they have any questions. Depending on the responses from the participants, they were briefly reminded about the study. Sometimes a detailed explanation was given if participants did not understand during the initial introduction of the study and in situations where the family carer was not present during the initial introduction of the study. If participants understood clearly what the study was about and were still interested in taking part in the study, they were asked to provide written consent (appendix 2). A checklist was administered to confirm that all criteria for study eligibility were met (appendix 3).

Figure 10 HIV clinic journey, recruitment strategy and study design for newly diagnosed patients with HIV/AIDS

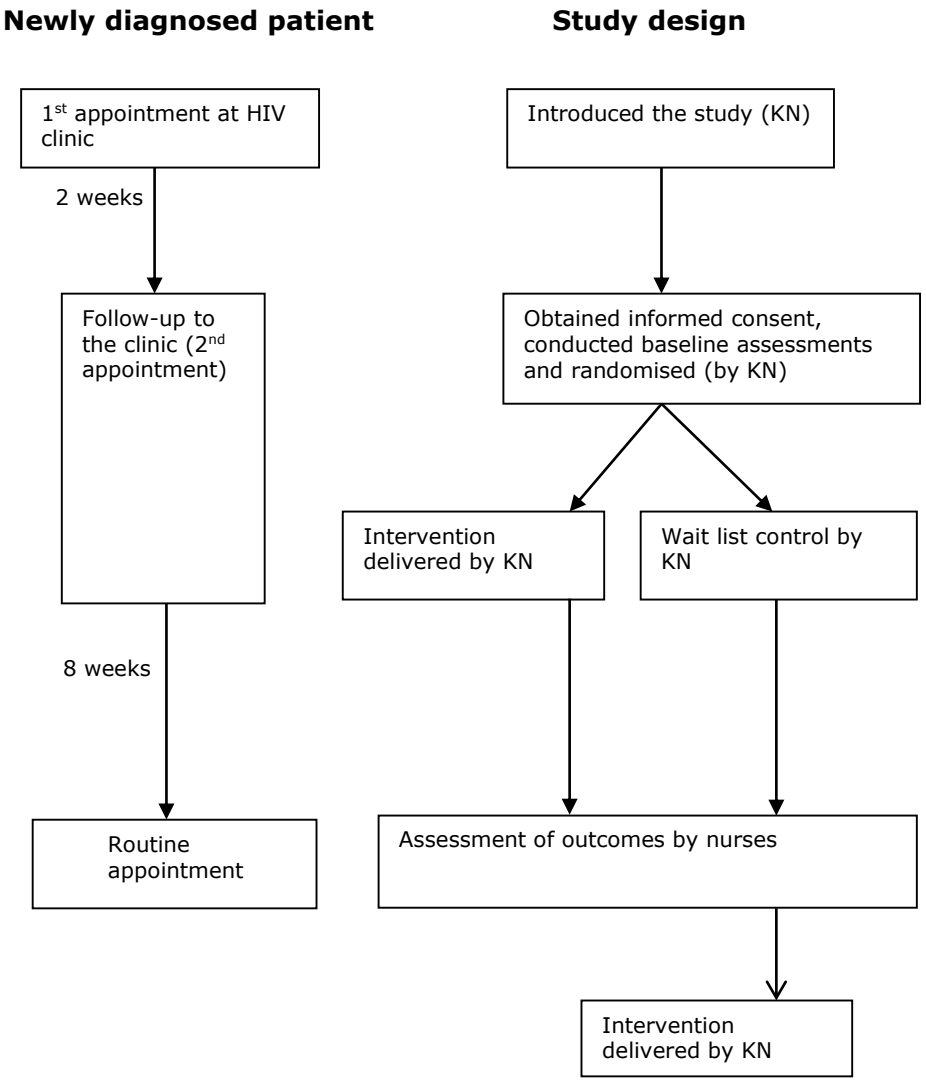
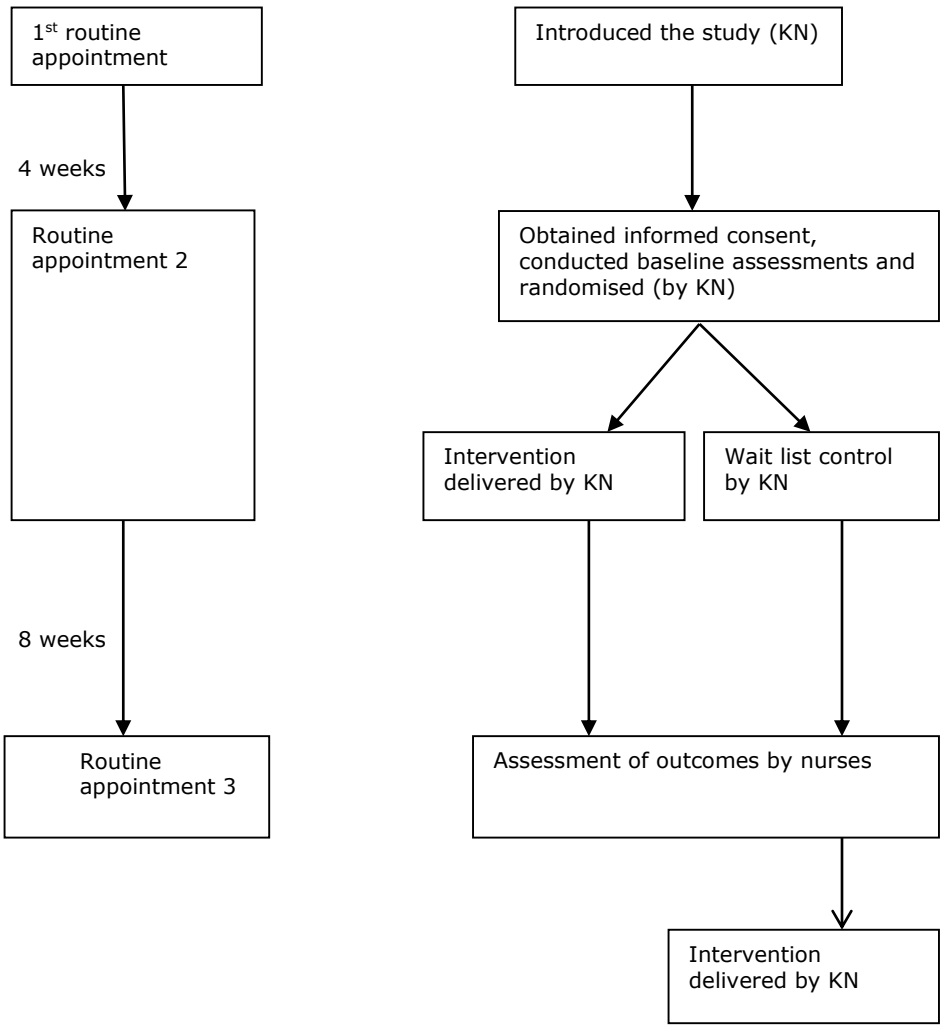


Figure 11 HIV clinic journey, recruitment strategy and study design for patients already on HIV treatment



6.6 Baseline assessments

After recruitment and obtaining written consent from participants, I conducted baseline assessments. Baseline assessments included the participants' details, demographic data, and date of diagnosis, current treatment, and presence of co-morbidities. Other baseline assessments conducted were in line with the outcome interests of the study which were: pain severity, pain interference, pain knowledge, quality of life, and motivation/rewards in providing care.

The pain education intervention study examined the effect of the intervention in terms of four patient outcomes (pain severity, pain interference, knowledge of pain management and quality of life) and three family carer outcomes (knowledge of pain management, quality of life and motivation to provide care). Patient outcomes are in line with IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) recommendation on core outcomes for patients with chronic pain (Dworkin et al., 2008, Dworkin et al., 2005b, Turk et al., 2003). The pain education intervention study randomised patient/carer dyads based on the findings from the two systematic reviews of educational interventions that there is insufficient evidence on the effectiveness of pain education interventions among patients with HIV/AIDS and family carers. The choice of instruments therefore was mainly based on the core outcomes used in clinical trials of pain management for patient and core outcomes in clinical trials among family carers of patients with chronic illnesses such as HIV/AIDS. The effect of HIV/AIDS related pain is experienced by both the person with HIV/AIDS and their carer and therefore the intervention targeted at improving outcomes for both. Therefore some

instruments such as the APCA African POS and patient/family pain questionnaires were administered to both the patient and family carer.

Table 14 Contents of baseline assessments

Participant	Area of assessment	Questionnaire	Mode of completion
People living with HIV/AIDS(PLWHA) (Patient participants)	Patient characteristics	Demographic information Clinical information	Face-to-face interview Review of medical records
	Perceived pain	Pain severity subscale (BPI-PS sub-scale) Pain interference subscale (BPI-PI-subscale)	Self-report
	Pain Knowledge	Patient pain questionnaire (PPQ-K subscale)	Self-report
	Quality of life	APCA African POS	Self-report
Family carers (carer participants)	Carers characteristics	Demographic information	Self-report
	Pain knowledge	Family pain questionnaire (FPQ-K subscale)	Self-report
	Quality of life	APCA African POS	Self-report
	Carers motivation	Picot Caregiver Rewards Scale	Self-report

6.6.1 Patient characteristics

Patient characteristics (Appendix 4) were gathered by asking a list of questions about demographic information including name, age, gender, marital status, education, religion, employment, address, date of referral, source of referral, and date of initial approach. Clinical information recorded included presence of co-morbidities such as TB, cancer, current pain treatment, CD4 count and HIV/AIDS clinical stage. These were obtained by extracting information from medical records.

6.6.2 Pain assessments

Pain severity was measured using the single item of the Brief Pain Inventory (BPI-PS) (Keller et al., 2004) where patients were asked to rate the severity of their pain over the last week in the domain of worst pain, least pain, average pain and pain right now (Keller et al., 2004). A rating was made on a zero to 10 scale with higher scores indicating greater severity of pain. This is consistent with the measurement of pain severity in a number of clinical trials (Cleeland, 2009). The BPI has been used with patients with cancer and other chronic illnesses such as HIV/AIDS (Vogl et al., 1999, Breitbart, 1996a) and to study the management of pain in South Africa (Beck and Falkson, 2001). The BPI has been linguistically validated in Afrikaans, Xhosa, Zulu in South Africa (Mphahlele et al., 2008, Cleeland, 2009) and has been used to study pain severity and prevalence in Uganda (Namisango et al., 2012) South Africa (Narasimooloo et al., 2011) Nigeria (Ebirim and Otokwala, 2013). Assessment of pain was made easier by the use of validated numerical rating scale with face validity (Huang et al., 2012).

Pain interference with daily activities was measured using the mean score of the seven pain interference items of the Brief Pain Inventory (BPI-PI). These items measure, on a scale of zero to 10, the degree to which the patient reports pain interfering with each of seven activities (general activity, walking, work, mood, enjoyment of life, relations with others, and sleep) and is the recommended method of assessment of pain-related functional impairment in clinical trials (Dworkin et al., 2005a) (Appendix 5). BPI has well established reliability: Cronbach alpha values ranges from 0.77 to 0.91, and it has been

translated into more than three dozen languages by examining the consistency of severity and impact of pain (Keller et al., 2004).

The BPI was chosen because it is easier to administer and simple to understand by patients. It takes between three to five minutes to complete (Cleeland, 2009). It can be self-administered by patients and it has been validated in sub-Saharan Africa among HIV/AIDS and cancer patients. The BPI is frequently used to assess pain in HIV/AIDS population. The BPI is the only validated instrument to assess pain interference with daily activities. BPI is relatively easy to translate into other languages for non-English speaking patients. It captures pain severity and impact of pain and improvement in pain after changes in analgesic prescription and implementation of new interventions or pain treatments. Unlike other instruments such as the Mc Gill pain questionnaire (Melzack, 1975), which is highly complex and potentially burdensome for patients who experience higher levels of pain.

6.6.3 Patient pain knowledge

For patients, knowledge of pain management was measured using the knowledge sub-scale of the Patient Pain Questionnaire PPQ-K (Ferrell et al., 1994). The PPQ-K is made up of nine items asking the patient to agree or disagree with statements about the effectiveness, timing of pain medication dosage, and adequacy of pain medication dosage. Agreement/disagreement is rated on a scale of zero to 10. Scores range from zero to 90 with lower scores indicating greater patient knowledge of pain management (Appendix 6). The

tool has been tested for reliability and validity. Content validity (CVI=.95), test-retest reliability (r=.65), internal consistency (alpha=.74), and factor analysis established with carers (N=219) (Ferrell et al., 1993b).

Although this instrument has not been validated in Africa and among HIV/AIDS patients, the questions are likely to be relevant to this population. For example, 'patients with a chronic illness can live a pain free life', 'Pain medications should be given only when pain is severe', 'It is better to give pain medication around the clock rather than only when needed'. The PPQ is not overly burdensome, and freely available for research use. There is a lack of validated instruments to assess pain knowledge among people with HIV/AIDS. In a pilot study to assess knowledge levels among HIV/AIDS patients Gifford et al (1998) created their own instrument due to a lack of instruments available to measure knowledge outcome among HIV/AIDS patients.

6.6.4 Patient quality of life

For patients, quality of life was measured using the APCA African POS patient sub-scale (Harding et al., 2010b). The APCA African POS consists of seven items relating to patient pain and symptom assessment, psychological, spiritual and emotional concerns. Possible scores (with questions 4,5,6 and 7 reversed) range from zero to 35 with higher scores indicating worse outcomes/quality of life. The tool has been developed and tested in three African countries (Powell et al., 2007).

The African Palliative Care Association (APCA) African Palliative Care Outcome Scale (POS): (Appendix 7) was developed in response to a lack of rigorously validated instruments to assess palliative care outcomes in people living with HIV/AIDS in Africa (Harding and Higginson, 2005). The tool was first developed in the UK and was tested and validated for monitoring and evaluating palliative care provision among patients with life limiting illnesses (Powell et al., 2007). The APCA Africa POS was piloted in three countries in Africa (South Africa, Kenya and Uganda) providing specialist palliative care services and results suggested that the tool can be used as a monitoring and evaluation instrument in palliative care services (Powell et al., 2007). Subsequently the tool was validated in five African countries (Malawi, Zambia, Tanzania, Botswana, and Zimbabwe) among 682 patients and 437 carers. Face validity showed that the tool mapped well to identified needs (N=90 patients, and N=38 carers), and cognitive interviews demonstrated good interpretation (N=73 patients and N=29 carers)(Harding et al., 2010b). APCA African POS was chosen because it is the only tool to have been validated in sub-Saharan Africa including Malawi among HIV/AIDS patients. It also has the advantage of being able to capture both physical and psychological aspects of pain.

The tool is simple and easy to administer, contains seven items and takes between two to five minutes to complete. Unlike other instruments that evaluate quality of life in HIV/AIDS such as HIV/AIDS targeted QOL (Holmes and Shea, 1998), QOL index (Ferrans and Powers, 1984) , and Medical outcomes study-HIV (Wu et al, 1993), which are complex, difficult to follow and quite lengthy. They have items ranging from 35-66 which require

considerable time to complete.

6.6.5 Carers characteristics

Carers' characteristics (Appendix 4) were gathered by asking a list of questions about demographic information such as name, age, gender, marital status, education, religion, employment, and address and carer/patient relationships.

6.6.6 Carer knowledge about pain management

For carers, knowledge of pain management was measured using the knowledge subscale of the Family Pain Questionnaire (FPQ-K) (Ferrell et al., 1993a). Like the PPQ-K, the FPQ-K is made up of nine items asking the carer to disagree or agree with statements about the effectiveness, timing of pain medication dosage, and adequacy of pain medication dosage. Agreement/disagreement was rated on a scale of zero to 10. Scores range from zero to 90 with lower scores indicating greater carer knowledge of pain management (Appendix 8). The tool has been tested with established reliability: test, retest and internal consistency, as well as validity: content, construct and concurrent. Content validity (CVI=.90), construct validity (ANOVA, $p<.05$), concurrent validity ($r=.60$, p. <.05), factor analysis and test-retest reliability ($r=.80$) established with a retest of carers (N=67) (Ferrell et al., 1995, Ferrell et al., 1993a). Like the PPQ, the FPQ was chosen because it is simple and easy to use and therefore likely to be well understood by family

carers. To my knowledge, it is the only validated tool available to assess carers' knowledge of pain management. Even though it was validated among family carers of cancer patients, the experiences and concerns of family carers of patients with pain associated with chronic illnesses are likely to be similar.

6.6.7 'Carers' motivation

'Carer' motivation was measured using the Picot Caregiver Rewards Scale (PCRS) (Fulton Picot et al., 1997). The PCRS is a 16-item scale measuring the positive consequences of caregiving. Respondents rate the degree to which items describe positive consequences of their caregiving on a 5-point Likert scale. Possible scores range from zero to 64 with higher scores indicating more positive caregiving experience (Appendix 9). The tool was psychometrically tested in a non-random sample of 83 black female caregivers and random sample of 256 black and white female and male caregivers. Alphas of 0.83 and 0.88 demonstrated acceptable internal consistency. Construct validity was demonstrated by support of hypothesized relationships with caregiving demands, palliative coping, depression and caregiver burden (Picot et al., 1997, Fulton Picot et al., 1997). The PCRS was chosen due to a lack of validated and available tools to evaluate carers motivation in providing care. I did an extensive search for instruments to assess carer motivation, but PCRS was the one that contained all the important aspects in the caregiving experience including feelings of happiness, family growth and strength, strength of relationships, and knowledge and skills. Other instruments such as

the Derogatis Stress Profile which measures total caregiver stress (Dobkin et al., 1991)**,** The Family Crisis Oriented Personal Scales which measures internal and external family coping (McCubbin and McCubbin, 1991), and global distress measured with the Brief Symptom Inventory (Derogatis and Melisaratos, 1983)**,** tend to focus on negative effects of caregiving such as stress, depression, anxiety. In contrast, the PCRS is easy to administer and language and content are kept simple. The individual items are likely to be understood by family carers of people living with HIV/AIDS. However the tool has not been validated in Africa, thus geographical setting and location can affect participant's responses due to differences in culture.

6.6.8 Carers' quality of life

For carers, quality of life was measured using the APCA African POS family sub-scale (Harding et al., 2010b). The APCA African POS consists of three items directed at carers addressing the adequacy of information the family has received, confidence in caring, and level of worry. Possible scores, (with questions eight and nine reversed) range from zero to 15 with higher scores indicating worse outcomes/quality of life (Appendix 7). Like the APCA African POS-patient sub-scale, the tool is easy to understand, taking the carer approximately a minute to complete. Other instruments that measure quality of life in family carers include the Tilden Interpersonal Relationship Inventory (Tilden et al., 1990), Hopkins Symptom checklist (Kaaya et al., 2002), and State-Trait Anxiety Inventory (Spielberger et al., 1983). However all of these instruments are quite long and contain items which were not the outcomes of

interest in the current study such as feeling nervous, worry about misfortunes, indecisive feelings, spells of terror, and feelings of being trapped.

6.6.9 Use of instruments in sub-Saharan Africa

While the BPI (Beck and Falkson, 2001) and APCA African POS (Harding et al., 2010b) have both been used previously in sub-Saharan African populations, use of the PPQ, FPQ and PCRS has been restricted to populations in western countries. Even though the PPQ, FPQ and PCRS have not been validated in Africa, my experience immediately prior to trial recruitment of piloting these scales as part of the questionnaires among 10 patients and 10 carers suggested that they were acceptable and understood by members of the population of patients and carers from which my sample was to be recruited. All the tools were translated into Tumbuka language by two experts. One conducted a forward translation and another backward translation; there were minor differences between the two translators and these were resolved by consensus (Cleeland, 2009)

Table 15 Summary of tools used for measuring outcomes

Concept/outcome	Name of Instrument	Scoring	Number of items	Validation
Pain severity	Sub-scale of the brief pain inventory (BPI)	0-40 with higher score indicating worse pain	4	Validated in more than three dozen languages by examining the consistency of its two factor structure (severity of pain, impact of pain)
Pain interference with daily activities	Sub-scale of the brief pain inventory (BPI)	0-70 with higher scores indicating worse interference with activities	7	As above
Patient pain knowledge	Sub-scale of the patient pain questionnaire (PPQ)	0-90, with a lower score indicating the most positive outcome and higher score indicating the most negative outcome	9	Evaluated among 85 cancer patients and family carers in California community hospital, cancer centre and community hospice
Patient quality of life	Sub-scale of the APCA African POS	0-35 with higher score indicating negative outcomes and lower score indicating positive outcomes	7	Pilot tested in three countries in SSA, validated in five countries in SSA among 682 patients and 437 family carers
Carers quality of life	Sub-scale of the APCA African POS	0-15 with higher score indicating negative outcomes and lower score indicating positive outcomes	3	As the APCA for patients above
Carers pain knowledge	Sub-scale of the family pain questionnaire (FPQ)	0-90 with a lower score indicating the most positive outcome and higher score indicating the most negative outcome	9	As the PPQ above
Carers motivation in caregiving	Picot caregiver reward scale (PCRS)	0-64 higher score indicating positive experience in caregiving	16	In the USA in a non-random sample of 83 black female caregivers and random sample of 256 black and white female and male caregivers

6.7 Randomisation

After baseline assessments, participants were randomly allocated to the pain education intervention group or usual care group**.** I implemented randomisation using a series of consecutively numbered, opaque, sealed envelopes. The envelopes were sent to me by post. Each envelope contained a study number and the arm ("INT" for intervention and "CON" for control groups) of the trial to which the participant was to be allocated. The envelope was opened in the presence of the participants after baseline assessments. Participants had a 50% chance of being allocated to either the pain education intervention group or usual care group. In order to limit imbalance between the treatment groups, participants were randomly assigned with block randomisation using the 'ralloc' command in Stata version 12 (StataCorp, 2011). This allocates participants at random in blocks of sizes 2, 4, 6, 8 and 10 with block sizes allocated unequally in the ratio of 1:4:6:4:1 (Pascal's triangle). The block size was hidden to me to avoid the possibility of predicting allocation at the end of each block (Pocock, 1983).

Randomisation was stratified by recruiting hospital. I was not involved in the preparation of envelopes and I was blind to block size. AA (my supervisor) generated the randomisation list, prepared the envelopes and had no contact with the study participants.

After assigning the participants into treatment groups, expectations were shared with them based on the groups they were allocated to. It was not possible for me and the participants to be blinded to individual allocations due to the nature of the study. The baseline assessments were conducted

before randomisation to minimise allocation bias. Clinic staff from the two recruiting centres were not involved in baseline assessments and were not aware of group allocation since all the participants were told not to tell anyone. Participants who were allocated in the intervention arm were told not to share the face-to-face discussion and leaflet with any other participant or clinic staff.

6.8 Interventions

6.8.1 Description of usual care/wait list

Both Ekwendeni mission hospital and Mzuzu central hospital have a palliative care clinic and HIV/AIDS clinic and care provided to HIV/AIDS patients was similar at the time of the study. All the participants in the trial received usual care. Both HIV/AIDS clinics conduct a health education session to all newly registered clients before they start treatment. The health education mainly focussed on description of HIV/AIDS medication, how HIV drugs work, and importance of treatment compliance, drug adherence and positive living. Assistance with pain management for patients with HIV/AIDS is currently provided by hospital-based palliative care nurses and typically delivered in either a palliative care clinic or HIV/AIDS clinic. Information relating to pain medication is typically responsive rather than proactive and ad hoc rather than systematic. Information was provided when requested by patients or carers. The focus was mostly restricted to pharmacological treatment of pain. Pain assessments were not usually conducted in a systematic way and not

recorded. It was unusual for this information to be shared with patients and/or their carers. Written information materials were not provided.

6.8.2 Description of the intervention

Patients randomly allocated to the intervention arm received the pain education intervention which I delivered. The intervention consisted of a leaflet (see appendix 13) and health education session delivered face-to-face to the participants at the HIV clinic or palliative care clinic (table 17 and table 18). The face-to-face session took approximately 30 minutes in a quite setting. A leaflet entitled "All about your pain" was given to participants who were given the opportunity to look through it (Nkhoma et al, 2015). I then discussed the contents of the leaflet with the participants and they were both encouraged to ask questions. After two weeks, participants received a phone call reminder to enquire whether they have any further questions after reading the leaflet. The phone call was made to remind the participants to make use of the intervention.

The pain educational intervention was underpinned and guided by the adult learning theory (andragogy) (Knowles, 1990, Knowles et al., 2005). Adult learning theory is defined as a collection and utilisation of several concepts and theories by which adult acquire knowledge and skills such as social cognitive theory, personality theory, humanistic theory (Rogers and Horrocks, 2010). Adult education has been recognised as the desirable process by which adults acquire knowledge and skills which brings about change in attitude and behaviour (Knowles et al., 2005).

Adult learning theory uses approaches to learning that are collaborative and problem-based. The theory emphasises equality between the teacher and the student (Dunn, 2002, Zoller and Harrison, 2007). The design of the leaflet and the structure of the intervention, the content and the mode of delivery enhanced proper discussion between me and the participants (patient and carer participants). The structure of the intervention allowed active participation of the patients and carers. This allowed them to freely ask questions and clarification and make contributions based on their previous knowledge and experience. These approaches facilitated knowledge acquisition and retention because of active involvement rather than just recipient of information. Based on this theory the intention of the pain education intervention was to reduce pain severity that patient experienced, improve their knowledge in assessing, classifying, and managing their own pain, this in turn enabled participants to know what to do when they are in pain or to actively make decisions about their own pain.

6.9 Development of a pain management information leaflet for people living with HIV/AIDS (PLWHA) and their family carers

Ideally complex interventions should be developed and implemented using a transparent and widely used framework such as the Medical Research Council (MRC) framework of evaluating complex interventions (Craig et al., 2008). Designing the study using the MRC framework will help to understand the mechanism of action of the intervention. Complex interventions are interventions that contain several interacting components

(Bennett and Closs, 2011, Craig et al., 2008); and may act both independently or interdependently (Campbell et al., 2000). They are widely used in health care services, public health and social sciences (Craig et al., 2008). In health care complex interventions may also be referred to as non-pharmacological interventions, because it is difficult to understand their mechanism of action, unlike pharmacological interventions which have a more easily identifiable way of exerting their effects. For example some pain drugs work by inhibiting the release of enzymes that transmit pain impulses, while non-pharmacological interventions like message or acupuncture affects the physiological action or psychological or a combination of both (Bennett and Closs, 2011). They are orientated towards physical, psychological, social, spiritual and clinical aspects of care. It is challenging to design and evaluate complex interventions to establish their efficacy and effectiveness (Bennett and Closs, 2011). In the current study I used the MRC framework to develop the intervention (an information leaflet) I involved health care workers (clinical officers and palliative care nurses), patients and family carers. A pilot study was conducted to assess the feasibility of the intervention. After piloting the intervention, the main study was conducted. However qualitative data were not gathered at the end of the trial to elicit participant's experiences of being part of the trial.

The design of the current study therefore makes it very difficult to explain if the mechanism is related to any of the change in outcomes observed. All that can be inferred from the design is that any change in outcomes observed is related to one or more components of the intervention rather than the action of individual and specific components.

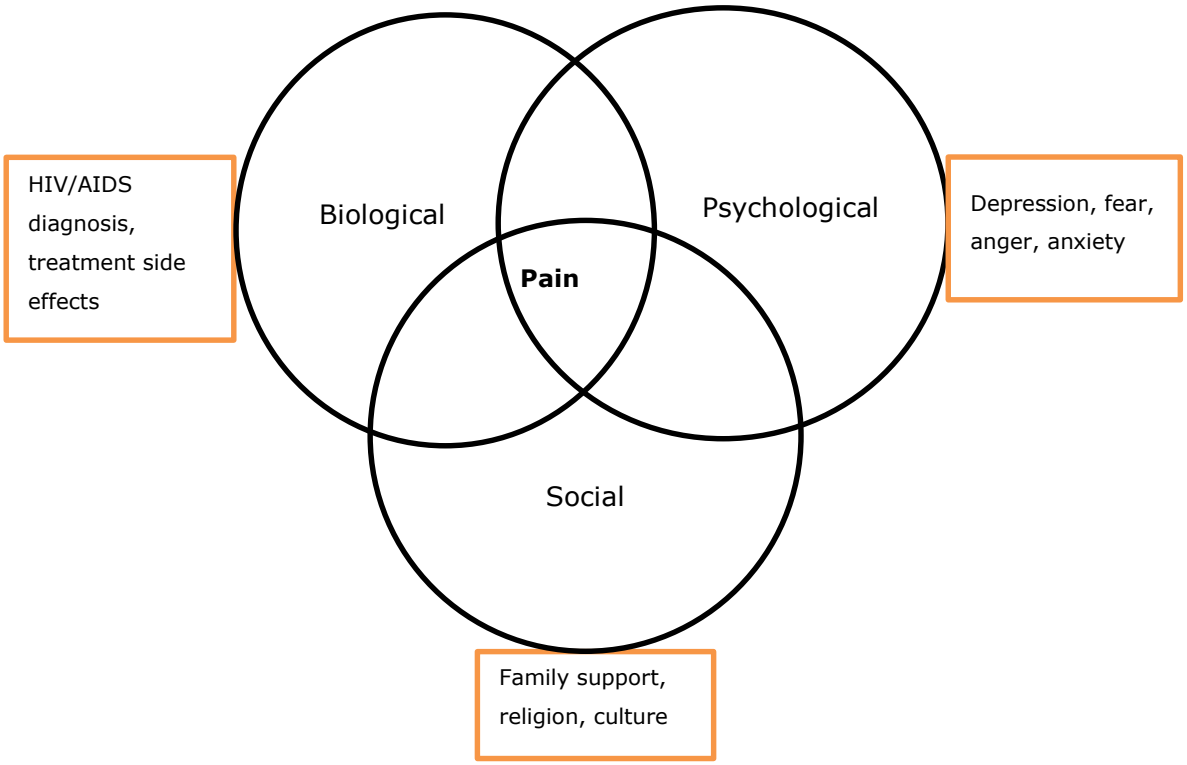
A leaflet was designed and developed which contained information about HIV/AIDS pain management for people living with HIV/AIDS. This was designed after looking at previous literature on cancer pain management (SIGN, 2009, Oldham and Kristjanson, 2004) and HIV/AIDS pain management in Africa (APCA, 2008, APCA, 2012) and pain management in Malawi (Ministry of Health, 2008b). The contents focused on definition of HIV/AIDS pain, causes of pain in HIV/AIDS, characteristics of pain in HIV/AIDS, beliefs and myths about pain in HIV/AIDS, beliefs and myths about pain medication, assessment of pain in HIV/AIDS, pharmacological management of pain, and non-pharmacological management of pain.

The biopsychosocial model (Engel, 1997) was used to guide the development of the pain education intervention. The biopsychosocial model (Figure 11) states that a human being has biological, psychological and social needs which have influence on illness and health (Frankel et al., 2003, Borrell-Carrió et al., 2004). Pain is a multidimensional phenomenon that includes physical, psychological, behavioural, spiritual, social, and economic components (Spross et al., 1990) and in agreement with this Dame Cicely Saunders describes this as a concept of total pain among terminally ill patients (Saunders and Sykes, 1993). Biological factors such as HIV cause AIDS which brings illness to an individual. HIV/AIDS is a chronic illness which eventually causes chronic pain. The diagnosis of AIDS itself brings psychological problems to an individual such as lack of self-control, anxiety, anger, stigma which further precipitates the condition. The social component such as lack of social support also worsens the condition (Borrell-Carrió et al., 2004). The management of HIV/AIDS requires a holistic approach because it is a chronic illness (Kell and Walley, 2009,

Parker et al., 2014). Even though the biopsychosocial model is criticised due to lack of structure that would facilitate analysis of weighted contribution of variables (Ghaemi, 2009), the model is useful in complex construct like pain in HIV/AIDS to explore the causes of HIV/AIDS pain and establish the appropriate and effective treatment (Parker et al., 2014).

This means that when managing pain in HIV/AIDS there is a need to provide pain relieving drugs to counteract the effects of biological processes, emotional care such as counselling and social support for instance presence of a family care. The pain educational intervention looked at all these components. The intervention involved a carer provider because HIV/AIDS patients in Malawi context need a carer provider from the time the illness is diagnosed until death. The clinic journey HIV/AIDS patients travel requires both medical and social interventions (Collins and Harding, 2007). The HIV/AIDS clinic journey (Figure 3 in chapter two and Figure 10 in chapter six) describes that carers of patients with HIV/AIDS are involved in managing the illness from the onset of the symptoms, the diagnosis of the illness and commencement of HIV treatment and continuation of HIV treatment for life.

Figure 12 The Biopsychosocial model of pain management



6.10 Patient and public involvement

During the development phase of the leaflet, five HIV/AIDS patients and their family carers were given a leaflet to read at home. They were asked to make comments of readability, content, understandability and design of the leaflet. They were given two weeks to read and discuss with family members and thereafter give feedback to me. Health care workers (three clinical officers, and four nurses) were also given the leaflet to read paying particular focus on the content, readability, understandability, components

and design. They were given one week to give feedback. All the patients, family carers were registered service users at Ekwendeni hospital. All health care workers were members of staff at Ekwendeni hospital. They provided feedback to me verbally through a face-to-face discussion.

Of the five patients and five carers who were given leaflets to read; four patients and four carers reported back to give feedback. Discussion about the feedback took place in a quiet setting with each patient and a family carer. All healthcare workers gave feedback and I had a face-to-face discussion with each healthcare worker.

6.10.1 Comments from patients and family carers

All the four patients and four carers were happy with the leaflet. They all expressed satisfaction with the contents of the leaflet, such as pictures and diagrams. All the participants reported that they understood the contents of the leaflet. There were no specific changes which they advised needed to be made.

6.10.2 Comments from clinical officers

Three clinical officers were consulted. All these clinical officers were providers of HIV/AIDS medication at Ekwendeni HIV clinic. In general they all expressed satisfaction with the leaflet because it covered all the issues relating to pain management in HIV/AIDS.

6.10.3 Comments from nurses

Four nurses were consulted. All these nurses were providers of HIV/AIDS medication; one was a palliative care nurse, three of which were also HIV positive themselves. They reported that the leaflet was somewhat useful to them personally because they also experienced pain symptoms due to HIV infection. *The content was clear 'I have personally started using it'.* (This nurse was referring to the fact that she started using the leaflet herself because she was also HIV positive and taking HIV medication). They were all happy with the contents and components in the leaflet.

6.10.4 Comments from home-based care Trainers/Coordinators

Apart from healthcare workers from Ekwendeni HIV clinic, health care workers from other institutions were also consulted. These are not only home-based care trainers at national level, but they also coordinate home-based care activities at their respective institutions. An email was sent to each one of them with a leaflet attachment. Two of them gave me feedback by email, but one of them gave me face-to-face feedback.

In general they were all happy with the intervention (leaflet) and made few comments and suggestions for example, avoid use of technical words such as 'Analgesics', this was replaced with a simple word '*pain medication'*, "Non-pharmacological interventions", was replaced with a simple sentence *"other ways of managing pain*".

The final version was made after incorporating all the comments from patients, family carers, home based-care providers, nurses and clinical officers.

The leaflet was in the form of a double sided A4 page, formatted and it could be gate folded into two to allow ease of use. It was printed in colour (Appendix 13). The contents included HIV/AIDS pain description, pain assessment, pain classification, pharmacological pain management and non-pharmacological pain management. The leaflet had several short sections under the following headings: HIV/AIDS pain description, pain assessment, World Health Organisation (WHO) pain management ladder, misconceptions about pain and pain medication, dispelling the misconceptions about pain and pain medication, pharmacological management of pain, non-pharmacological management of pain and principals of pain management. Photos, pictures and diagrams such as pain diagrams, pain scales, WHO analgesic ladder were used to enhance understanding about pain location, classification and pain rating. The WHO analgesic ladder also helped participants to appreciate the rating of pain and approaches to treatment based on the classification of pain. A trial (Mansoor and Dowse, 2007) reported that a simple written leaflet information with pictograms improved knowledge and understanding significantly among HIV/AIDS positive patients compared to two groups who received written leaflet information only and no information (usual care).

The leaflet was designed to be short, simple, and easy to understand. A Flesch Reading ease (Flesch, 1948) was calculated. This calculates how easy the material is to read and understand, a higher score indicate

material that is easier to read and understand and lower score indicate material that is difficult to read and understand (Flesch, 1948, Walsh and Volsko, 2008). Readability scores are useful in assessing overall ease of understanding written information (Murphy et al., 1994). Readability score states that 0-30% can easily be understood by a university graduate, 60-70 can easily be understood by a 13 to 15 years old student and 90-100% can easily be understood by a 11 year old student (table 16). For this leaflet, the readability score ranged from 67.1 to 80.3%. Each section of the leaflet was pasted into a Flesch Reading ease calculator and a score was obtained. Some authors (Mwingira and Dowse, 2007) reported that simplified patient written materials are more likely to be accepted and used.

Table 16 Readability score and interpretation

Score (%)	**Notes**
90-100	Easily understood by an average 11 year old student
60-70	Easily understood by 13 to 15 years old student
0-30	Easily understood by a university graduate

The intervention was delivered after completion of baseline assessments. Patients and family carers were each given a copy of the leaflet and were allowed to browse through briefly. Thereafter each section was read to the participants and explanations were made in the process. Practical advice was given and participants were allowed to ask questions or clarifications and all these were discussed. The components of the interventions are summarised in Table 17. The leaflet was developed in line with three issues that are supposed to be addressed when creating patient materials; purpose, collaboration and design (Ivnik and Jett, 2008).

In order to minimise contamination between the two treatment arms of the trial, a leaflet was put in the bag or hand luggage of the participant and the carer before they left the room where the intervention was delivered. Participants were strongly advised not to share the information discussed with anyone else and not to share the information leaflet with friends and health care workers.

Table 17 Components of the pain education intervention

Topics covered	**Content**
Introductions	Participants (patient and carer) welcomed Introductions and clarifications as required Leaflet provided and participants given time to read through
Overview of pain in HIV/AIDS	Pain defined in relation to HIV/AIDS Possible causes of pain in HIV/AIDS discussed Characteristics of pain relating to HIV/AIDS
Beliefs and myths about pain in HIV/AIDS	Participants given opportunity to share beliefs about pain in relation to HIV/AIDS Where appropriate misconceptions dispelled
Beliefs and myths about pain medication	Ask the participants' beliefs about use of pain medication Summarise and dispel misconceptions as required about pain medication
Assessment of pain in HIV/AIDS	Demonstrate with the help of body diagrams how to locate and describe pain Demonstrate use of pain assessment tools to rate and record pain Demonstrate with pain diagrams how to classify pain Explore type of pain experienced and strategies used to manage pain Discuss ways in which pain may be managed more effectively
Pharmacological management of pain	Demonstrate, using WHO analgesic ladder, how pain is managed with medications Give examples of available drugs used on WHO ladder Discuss most effective timing of pain medication
Non-pharmacological management of pain	Identify what non-pharmacological interventions participants are aware of and use Practical demonstrations on use of non-pharmacological interventions as appropriate
Other items covered	Participants given further opportunity to clarify any of the points discussed Participants encouraged to re-read the leaflet after the end of the face-to-face meeting and refer to it whenever the patient experiences pain Advise participants to ask for clarification about the leaflet and its contents by sending a missed call to KN who will then return the call Routine follow-up call at two weeks

The pain management ladder was explained to the patients and family carers so that they should know how pain is rated and managed depending upon the severity of the pain. Patients and carers were informed which drugs are appropriate as severity of pain increases. This information was given to the participants in the pain education intervention to make sure that they should explain to the doctor that their pain is either mild, moderate or severe. They were further informed that should the pain be moderate or severe they should seek medical attention and explain to the doctor that they need strong analgesia. Presumably this influenced the way doctors prescribed the analgesia. The pain ladder is used by doctors and nurses to prescribe, however this was extended to patients/carers as a way empowering them with basic knowledge on pain management. In Malawi usually doctors and nurses do not communicate to the patients and families about drugs. Therefore the pain education intervention was designed to provide information to the patients/families despite the fact that they cannot self-prescribe.

The features of usual care and the pain education intervention are described in Table 18 below to differentiate the usual care from the intervention in terms of content, method of delivery, content and general description (Guo et al, 2012).

Table 18 Features of Usual care and educational intervention

Element	Usual care/wait list control	Intervention
General description	Unstructured verbal information	Leaflet based information, advice, explanation and discussion
Form	General information on the treatment prescribed and instructions to be followed, responsive information from palliative care nurses	Information leaflet distributed "All about your pain" including 30 minutes face-to-face verbal instructions and advice on pain assessment and management.
Content	General information about HIV/AIDS medication and treatment compliance	Specific information about procedure on pain assessment and classification using pain scales and pain diagrams, including pain management using WHO analgesic ladder and specific drugs on each step. Description in relation to the model: (1)Biological-infection with HIV and side effects of treatment (2) Psychological-depression, anger , fear and anxiety effects of HIV/AIDS (3) Social-availability of family and spiritual support.
Written materials	None	Leaflet with simplified text information and diagrams, pictures/photos for quick reference.
Method of delivery	General staff members	KN

6.11 Pilot study

Before recruitment for the main study begun, a pilot study was conducted to assess delivery of the intervention, understandability of the questionnaires and intervention and feasibility of the study. Ten patients and ten family carers were recruited for the pilot study. They were followed-up after four weeks (one month) after delivery of the intervention.

Six patients and their family carers were randomly allocated to the pain education intervention and they all received the face-to-face discussion and a leaflet. Four patients and their family carers were randomly allocated to the usual care group and received the leaflet upon completion of follow-up assessments. Of the ten patients/carer dyads, nine patients and six family carers were followed-up after four weeks; (meaning six patients/carer dyads and three patients without their family carers were followed-up) and one patient and four family carers were lost to follow-up. The reasons for loss to follow-up were patient and carer having transferred to another centre (n=1), no transport for the carer (n=3). All the participants who completed follow-up assessments were happy with the intervention and reported that they did not share the leaflet with anyone else.

6.11.1 Lessons learnt from pilot study

Even though the pilot study was conducted with the aim to test the questionnaires and for me to practice how to administer the intervention, I learnt some lessons from this exercise as outlined below which helped in all the stages of data collection for the main study:

- Patients who have been on HIV treatment for a period of 12 months and above and showed to be compliant and adherent to treatment guidelines and standards were able to come to the clinic without their family carers, and in some cases only the family carer could come (on behalf of the patient) to the clinic to collect HIV medication for the patient. These patients were also given a drug supply that could last three or four months, and therefore this meant they did not require to come to the HIV clinic until

after their treatment has been completed, unless they developed a problem which required medical attention before the scheduled date of follow-up. While this is good development for the patient because in this case they did not have to spend transport (for two people) and it could mean the carer provider could do other things at home, however this was a challenge to me because I needed both the patient and the family carers as study participants in the trial. The longer period of follow-up (three to four months) for these patients who were adherent to treatment was also not in line with the design of this trial (two months follow-up). I therefore recruited mostly newly registered patients because new patients had two weeks or one month follow-up schedules to the HIV clinic (figure 10).

- Recruitment was slow during the pilot phase of the study. It took almost one month to recruit ten patients/family carers dyads. This concerned me because it meant that the main study would take longer to complete than originally anticipated. In response to this I made contacts with another centre in advance so that should there be a need to extend the study to another site, I would have things already in place.

- Some participants were not able to understand how to rate pain on the visual analogue scale (zero to 10) or (zero to five) and therefore to assess for pain severity posed a challenge. I therefore made a print out of the universal pain assessment scale diagram for participants to see the facial diagrams and compare themselves with what they see in order to rate their pain. This proved to be easy for them to rate their own pain and therefore I utilised this process for all the pilot work participants and for the main study. Outcome assessors were also trained to conduct assessments in a similar manner.

- Initially there was no plan to make a follow-up phone call reminder to the participants randomised to the intervention group, however some participants reported that they wanted to ask for clarification a few days after they received the intervention, but they could not call me because they did not have credit. I therefore included a two weeks follow-up phone call reminder as one of the ingredients of the intervention in order to check if participants have questions after receiving the intervention and also to encourage and remind them to read the leaflet provided.

6.12 Outcome measurers

In this section I describe how the follow-up assessments were scheduled and conducted among study participants randomised to either the pain education intervention or usual care groups. Follow-up measures were conducted after eight weeks following delivery of the intervention. Two nurses' blind to the groups conducted the follow-up assessments. There were two nurses who conducted follow-up assessments one from each recruitment centre. This was implemented during the routine appointments to the HIV or palliative care clinics. Follow-up assessments were conducted using the same assessments tools described in baseline assessments on both the patients and carers.

The primary outcome was average pain severity measured by a subscale of the brief pain inventory (BPI-PS) since the intervention was designed to evaluate the effects of pain education on reducing pain severity, therefore pain score was the main focus of this study. The secondary outcomes were: For patients; pain interference with daily activities measured by a

subscale of the BPI-PI, patient pain knowledge measured by a subscale of the Patient Pain Questionnaire (PPQ-K), patients quality of life was measured by a subscale of the APCA African POS. For carers; knowledge of pain management was measured using the knowledge subscale of the Family Pain Questionnaire (FPQ-K), carer motivation was measured using the Picot Caregiver Rewards Scale (PCRS) and carers quality of life was measured using the subscale of the APCA African POS. I was not present during the follow-up assessments to prevent influencing responses from participants. After follow-up assessments were completed a leaflet was given to participants who were randomised to the wait list control group. A detailed face-to-face discussion was not provided. On exit from the trial participants who were randomised to the wait list control group were advised to read the leaflet and they were asked not to share it with anyone else because the study was still ongoing. Those participants who were randomised to the pain education intervention were advised to continue referring to the leaflet and they were reminded not to share it with anyone else because the study was not yet completed.

A range of secondary outcomes were chosen due to the complex nature of the intervention (Bennett and Closs, 2011). In complex interventions we need to have a number of outcomes to be measured, unlike in drug trials which usually have biomedical or physiological outcomes (Roland and Torgerson, 1998a). A pragmatic trial measures the effectiveness of the intervention, that is the benefit the new treatment will produce in routine care of the patients. The design of pragmatic trials reflects variations between patients that occur in real clinical practice and they aim to inform practice which treatment is better than the other (Roland and Torgerson,

1998b). The pain education intervention study tested the effect of education intervention consisting of an information leaflet, face-to-face discussion and phone call reminder compared to usual practice in a real world population. Although the challenge in conducting pragmatic trials is the need for more outcomes as well as more participants because increasing the number of outcomes increases the probability of reaching statistical significance by chance (Roland and Torgerson, 1998a).

Patient outcomes are in line with IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) recommendation on core outcomes for patients with chronic pain (Dworkin et al., 2008, Dworkin et al., 2005b, Turk et al., 2003). The time point between delivery of the intervention and follow-up assessments was chosen to be consistent with other studies of pain education (Clotfelter, 1999, Hudson et al., 2005) and based on recommendations from pain research experts (Bennett and Closs, 2011).

6.13 Sample size

A power calculation was based on the primary outcome of average pain severity on the BPI (Keller et al., 2004). To be able to detect a mean difference of 10% between the treatment groups in the primary outcome measure (average pain severity in the BPI). A 10% improvement is the difference considered the lower limit of changes considered clinical important (Dworkin et al., 2008). Using a p-value cut-off of 0.05 to determine a statistically significant result, it was calculated that 76 people per arm of the trial were needed to complete the study to give 80% power

to detect such a difference. This is based on a review (Bennett et al., 2009) that suggests that education-based interventions are able to produce this level of improvement in pain reduction, and that a standard deviation of 2.2 points is a liberal estimate of variability. To allow for 15% attrition, I aimed to recruit 182 participants to the trial. However I did not power secondary outcomes in this study.

Power was calculated using the following formula for minimal sample size:

$$\frac{(u+v)^2(\sigma_1^2+\sigma_2^2)}{(\mu_1-\mu_0)^2}$$

Where

1. u is the one sided percentage point of the normal distribution corresponding to 100% minus the power; using 80% power this relates to the one-sided percentage point of 20% (100-80), u = 0.84.
2. v is the percentage point of the normal distribution corresponding to the (two-sided) significance level; using 5% level of significance, v = 1.96.
3. σ_1 and σ_2 are the standard deviations in each of the treatment groups; assumed to be the same (2.2 points or 22 on a scale of 0 to 100).
4. $\mu_1 - \mu_0$ is the difference between the two means; 10% was the difference considered clinically relevant to detect (or 1 on a scale of 0 to 10).

$$\frac{(0.84 + 1.96)^2(2.2^2 + 2.2^2)}{(1)^2} = 75.89 \approx 76 \text{ per arm}$$

6.14 Data Management

Each participant had an assessment form (questionnaire) conducted at baseline by myself and at follow-up by the nurses. Nurses who conducted follow-up assessments returned the questionnaire the same day after completing assessments. Every participant was given a trial number (ID number). Each questionnaire had an ID number corresponding to the participant ID number. Firstly each questionnaire was checked for missing responses. Data was then entered into Microsoft excel spread sheet blind to the participants group allocation. Data were stored on a personal password secured computer and university password secured computer. All data were only accessed by my supervisors and I.

6.15 Data analysis plan

The principles guiding the data analysis for the study were (i) minimisation of bias; (ii) transparency; and (iii) drawing statistical inference that was true to both study design and data.

Data was entered into a spreadsheet with allocation codes kept separately and linked only by a unique identifier for each patient/carer dyad. These spreadsheets were converted into Stata version 12 datasets (StataCorp,

2011). A series of sequential Stata 'do' files (Appendix 15) were used to conduct the analysis and ensure that there was a clear audit trail of data cleaning and production of results. Each Stata 'do' file was used for a specific element of the analysis:

1. Organisation of variables and generation of derived variables
2. Data cleaning
3. Encoding string variables
4. Transposing outcome variables
5. Ordering new variables (patient/carer baseline/follow-up)
6. Producing output for baseline tables and figures
7. Analysis of outcomes
8. Sensitivity analysis and checking model assumptions

The two treatment groups were examined at baseline in terms of demographics, recruiting centre, and baseline values of all study outcomes. Categorical variables are presented using frequencies and proportions, and continuous variables are presented using means and standard deviations.

There was no formal testing of differences at baseline. This was deliberate and in accordance with the detailed consort guidelines (Moher et al., 2010) The authors of the guidelines argue that testing of baseline differences for the probability of them being observed by chance is both superfluous and potentially misleading as the process of randomisation means that by definition, baseline differences are due to chance.

All patients and family carers were analysed according to the group they were randomised to. This approach is sometimes referred to as 'modified intention-to-treat' as the use of strict intention to treat analysis is only possible where there is no loss to follow-up (Abraha and Montedori, 2010, White et al., 2011). This approach was used for all seven outcomes. It involved analysing all the participants as originally allocated to either pain education intervention group or usual care group. Lost to follow-up participants were excluded from the analyses.

To minimise bias and ensure that all analyses was carried out according to the protocol (Nkhoma et al, 2013) and not driven by results, 'do' files were built using a randomly generated variable for 'arm 1' and 'arm 2'. Only once outputs were available to populate tables and figures was this variable replaced by the original variable that determined which dyads were allocated to which randomised group.

Treatment groups were compared in terms of the primary outcome measure (pain severity using the BPI-PS treated as a continuous measure) using a linear regression model with baseline BPI and treatment group and recruiting centre as covariates. Adjusted analysis were also conducted for primary outcome measure (average pain severity using BPI-PS treated as a continuous measure) using linear regression model with baseline BPI, treatment group, recruiting centre, age and gender as covariates:

$$yi = \alpha + \beta 1xi + \beta 2xi + \beta 3xi + \beta 4xi + \beta 5xi + \varepsilon i$$

where *yi* is the BPI-PS outcome and *β1* to *β6* are baseline BPI, treatment group, recruiting centre, age and gender for an individual (i) and ε is the error around the prediction.

Analysis of each of the six secondary outcomes (BPI-PI, PPQ-K, APCA African POS patient score, FPQ-K, PCRS, APCA African POS carer score) was conducted using six equivalent models with estimates of treatment effect conditional on the value of the outcome at baseline.

To test for any violations of the assumptions of linear regression, residuals were calculated in Stata using the 'predict' command. This calculates the difference between the fitted values for each participant and the actual outcome value. These were then plotted to examine for departures from the assumption of normally distributed residuals that would undermine any conclusions inferred from the models.

The only post-hoc analysis undertaken was that involving medication use. This was in an attempt to unpick the mechanism whereby pain education might lead to improved outcomes. Treatment groups were compared in terms of use of analgesia for treatment of pain at follow-up adjusting for baseline pain medication, recruitment centre, age and gender. Treatment groups were also compared in terms of type of medication received at follow-up adjusting for medication use at baseline, recruitment centre, age and gender using a logistic regression model.

Sensitivity analysis was performed as follows: I conducted secondary analyses that (1) adjusted for variables which were considered potential predictors of outcome (age, gender, number of pain medications at baseline) assuming missing at random and (2) considered plausible scenarios for departures from the missing at random assumption using the Stata command 'rctmiss' (White et al., 2011). These scenarios were for all outcomes using scores of the mean outcome plus and minus 50 points for

both arms and individual arms. All models included recruitment centre as a covariate.

All analyses were conducted using Stata version 12 (StataCorp, 2011). All reported P values are two-tailed, with $P<0.05$ considered statistically significant.

6.16 Ethical considerations

Ethical approval for this study was obtained from the University of Nottingham Medical School Ethics Committee (SNMP 11042012) (Appendix 10) and the National Health Sciences Research Committee of Malawi (Appendix 11). The study was registered by Current Controlled Trials ISRCTN72861423 in October 2012. The protocol for this study has been published (Nkhoma et al., 2013) appendix 15.

Carrying out research among participants with a chronic illness like HIV/AIDS raises a number of ethical issues. People living with HIV/AIDS and their family carers experience physical, social, psychological and spiritual problems. They are therefore considered a vulnerable group of people and require special attention in relation to research (Addington-Hall et al., 2007). The following ethical issues were carefully considered when designing and implementing the study.

- The principle of beneficence which stipulates that the researcher should come up with strategies to minimising harm, but maximise benefits (Polit

and Beck, 2008). There was no physical harm in this study because the trial did not involve invasive procedures in technical sense, so the risk of harm was low; however possibly there was psychological harm, because the participants had to contribute their time to be involved in the study. In addition participants in the control group had to wait for two months before they received the intervention. However since the study evaluated the effectiveness of the education intervention, I needed a control group in order to come up with conclusive results and evidence. In line with this (Polit, 2006, Medical Research Council, 2005) argues that considering risk versus benefit ratio the study is ethical because the outcomes of the study are expected to inform policy and practice in the management of HIV/AIDS pain in patients' homes.

- Participant's right to decide whether or not to take part in the trial was respected. There were no rewards for participants who decided to take part in the study. Participants were given information sheets about the study. These were available in both English and Tumbuka, the local language in Malawi. The language used was simple and clear (Cormack, 2000). The information sheets explained details about the study aims and objectives. Participants who took part in the study were given an informed consent, they were fully informed that they have the right to withdraw from the trial at any time without giving reasons and that this was not going to affect their routine care. Data were privately, confidentially stored in a password protected personal and or university computer. Data was not shared with any person apart from my supervisors; each participant was assigned an identification number which was used to collect baseline and follow-up assessments.

- The question of equipoise was also taken into consideration. This refers to genuine uncertainty that treatment in one arm of the trial is superior over treatment from the other arm of the trial (Djulbegovic, 2007, Mann and Djulbegovic, 2003). It was not known whether the pain education intervention was effective among this population and it was not part of routine care. Therefore, no patients or carers were denied a treatment through random allocation that they would normally get under the current service arrangements. To avoid disappointment for those not randomised to the pain education intervention, the intervention was also delivered to those randomised to usual care on completion of the trial. Equipoise did exist in this study because previous studies reviewed have not produced evidence that pain education interventions are effective in the population of HIV/AIDS and their family carers (Millard et al., 2013). It would have been unethical and unnecessary to conduct this study if I was certain that pain education interventions are effective in HIV/AIDS (Djulbegovic et al., 2000).

  In order to ensure that participants were not burdened greatly due to taking part in the study, the intervention was kept simple and short, the questionnaires were short.

6.17 Chapter summary

This thesis is based on a randomised controlled trial evaluating the effects of a pain education intervention (consisting of a face-to-face verbal discussion, an information leaflet and follow-up phone call reminder at two-weeks) on pain severity and pain management among HIV/AIDS patients

and their family carers. The intervention was specifically designed to improve pain severity and pain management among HIV/AIDS and family carers. The study design included developing a leaflet on pain management titled "All about your pain" through consultations with patients, family carers, and healthcare workers involved in care provision to HIV/AIDS patients, and piloting the tools and the intervention. The design of the intervention was guided by the bio-psychosocial model and the adult learning theory was used to deliver the intervention. Due to the design of this study, it is difficult to know how an education intervention leads to pain improvement among patients and carers. However when patient/carer dyads experienced pain or perceived pain they were taught how to rate the pain, classify the pain, use self-management interventions and how to seek medical care.

Adult HIV/AIDS patients and their family carers were randomised to either usual care/wait list control group or 30 minutes face-to-face verbal instructions and discussion on pain management, augmented by a leaflet and a phone call reminder after two weeks group. The primary outcome was average pain severity measured by a sub-scale of the BPI. Secondary outcomes for the patient were pain interference with daily activities of living measured by the sub-scale of BPI, patient pain knowledge measured by a sub-scale of the patient pain questionnaire, patient quality of life measured by a sub-scale of the APCA African POS. Secondary outcomes for the carers were pain knowledge measured by a sub-scale of the family pain questionnaire, quality of life measured by a sub-scale of the APCA African POS and carers motivation measured by Picot Caregiver Rewards Scale.

Baseline measurers were conducted two to four weeks after introducing the study to potential participants while follow-up measurers were conducted eight weeks after randomisation. The next chapter presents the results of the trial.

CHAPTER SEVEN: TRIAL RESULTS

7.1 Introduction

This chapter reports the results of the pain education intervention trial. The recruitment and flow of participants, the baseline characteristics of the study participants in the two arms of the trial are described. I describe the uptake and adherence of the participants to the intervention. The follow-up assessments at eight weeks after randomisation and delivery of the intervention are reported. In this chapter I report the differences observed in primary and secondary outcomes between the two arms of the trial.

7.2. Recruitment and flow of participants

The period of recruitment for the trial was between September 2012 and June 2013. A total of 308 participants were approached of which 126 (40.9%) were excluded on the basis of being unable to read or write (n=15), had no carer provider (n=45), were outside the catchment area (n=15), were cognitively impaired (n=4) or the patient had died before recruitment (n=10). Of the remaining 219 participants, 37 (16.9%) of them declined to participate. In total 182 patient/carer dyads were recruited to the trial. Participant flow through the trial is illustrated in Figure 12.

Figure 13 Flow diagram of the progress through the phases (enrolment, randomisation/intervention allocation, follow-up and data analysis) of the two arms of the trial

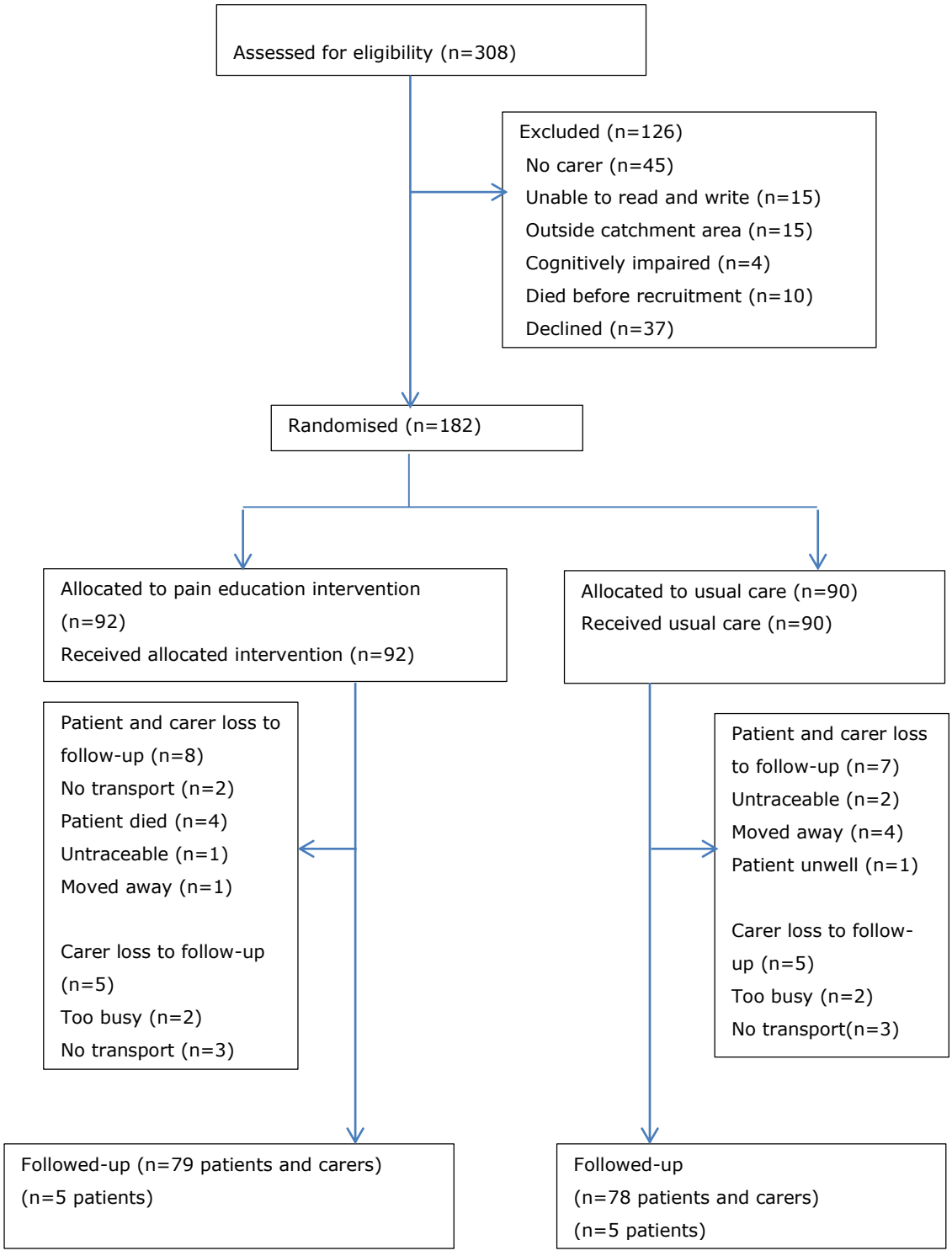


Table 19 Baseline characteristics of patient participants (n=182) randomised to the pain education intervention and usual care

Values are numbers (percentages) unless stated otherwise

Variables	Pain education intervention (n=92)	Usual care (n=90)
Mean (SD) age in years	40.48 (11.30)	41.31 (11.65)
Male/Female	43 (46.74)/ 49 (53.26)	56 (62.22)/ 34 (37.78)
Marital status		
Married	61 (66.30)	58 (64.44)
Single	11 (11.96)	13 (14.44)
Divorced/separated	11 (11.96)	10 (11.11)
Widow/widower	9 (9.78)	9 (10)
Education		
Primary school	21 (22.83)	14 (15.56)
High school	66 (71.74)	72 (80.00)
College/University	5 (5.43)	4 (4.44)
Occupation		
Farmer	26 (28.26)	28 (31.11)
Civil servant	13 (14.13)	12 (13.33)
Housewife	14 (15.22)	6 (6.67)
Unemployed	6 (6.52)	1 (1.11)
Student	5 (5.43)	4 (4.44)
Skilled manual	8 (8.70)	8 (8.89)
Retired	1 (1.09)	1 (1.11)
Admin workers	2 (2.17)	2 (2.22)
Small scale business	10(10.87)	13 (14.44)
Other	7 (7.61)	15 (16.67)
Religion		
Christianity/Islam	88 (95.65)/ 4 (4.35)	87 (96.67)/ 3 (3.33)
Recruitment centre		
Ekwendeni/Mzuzu	53 (57.61)/ 39 (42.39)	53 (58.89)/ 37 (41.11)
BPI Average pain severity mean (SD)	50.76 (24.86)	51.22 (27.10)[a]
BPI Pain interference mean (SD)	49.91 (27.97)	49.46 (29.48)[b]
PPQ-K subscale Pain knowledge mean(SD)	67.78 (16.61)	66.24 (18.84)[c]
APCA African POS subscale mean (SD)	44.78 (22.79)	48.92 (20.50)[d]

[a] BPI average pain severity: scores range from 0-10; higher scores representing positive outcomes

[b] BPI pain interference: scores range from 0-70; higher scores respresenting positive outcomes

[c] PPQ: scores range from 0-90; higher scores representing positive outcomes

[d] APCA African POS: scores range from 0-35; higher scores (with some items reversed) representing positive outcomes

7.3 Baseline characteristics

Baseline data were collected from all 182 patients and 182 carers before they were randomly allocated to either the pain education intervention group (n=92) or the usual care group (n=90). Table 19 and Table 20 summarises the comparison of the two groups of patient and carer participants in terms of demographic and clinical characteristics at baseline.

7.3.1 Patient characteristics

At baseline the mean age of patient participants in the two treatment groups were similar (40.5 years in the pain education group and 41.3 years in the usual care group). There were fewer men in the pain education intervention group (43/92) compared with the usual care group (56/90). There were no obvious differences between the two groups in terms of marital status. However, those in the usual care group tended to be more educated with only 14 of 90 patients having received no further education beyond primary education compared with 21 of the 92 patients in the pain education group.

There were no differences between the two groups in terms of occupation except that the pain education intervention group included twice as many housewives (14/92 versus 6/90 in the usual care group), and more patients with no employment (6/92 versus 1/90 in the usual care group). There were no differences in religious background between the two groups. At baseline, patients allocated to the usual care group had a slightly higher mean quality of life score as measured by the APCA (African Palliative care Association) African POS (Palliative care outcome score). The mean APCA African POS was 4.14 higher in the usual care group than in the pain

education intervention group (48.9 compared with 44.8). Both groups had similar mean scores at baseline in terms of average pain severity, pain interference, and patient knowledge of pain management.

In summary the two groups of patients had similar characteristics in terms of age, marital status, and religion; however they had some differences in terms of gender ratio, education and employment status. Participants in the pain education intervention were less likely to be male, but more likely to be female, and less likely to be educated beyond primary education. Both groups of patients had similar mean scores at baseline regarding average pain, pain interference and knowledge. Patient reported quality of life was slightly better among patients in the usual care group.

Table 20 Baseline characteristics of carer participants (n=182) randomised to the pain education intervention and usual care

Values are numbers (percentages) unless stated otherwise

Variables	Pain education (n=92)	Usual care (n=90)
Mean (SD) age in years	41.12 (11.70)	42.62 (SD 11.40)
Male/Female	14 (15.56)/76 (84.44)	19 (21.11)/71 (78.89)
Marital status		
Married	78 (84.78)	81 (90)
Single	10 (10.87)	6 (6.67)
Divorced/separated	1 (1.09)	1 (1.11)
Widow/widower	3 (3.26)	2 (2.22)
Education		
Primary	21 (22.83)	22 (24.44)
High school	66 (71.74)	64 (71.11)
College/University	5 (5 .43)	4 (4.44)
Occupation		
Farmer	32 (34.78)	30 (33.33)
Civil servant	5 (5.43)	5 (5.56)
Housewife	24 (26.09)	30 (33.33)
Student	5 (5.43)	1 (1.11)
Skilled manual	2 (2.17)	3 (3.33)
Admin workers	3 (3.26)	5 (5.56)
Small scale business	13 (14.13)	8 (8.89)
Other	8 (8.70)	8 (8.89)
Religion		
Christianity/Islam	88 (95.65)/4 (4.35)	89 (98.89)/1 (1.11)
Carer relationship to patient		
Spouse	35 (38.04)	44 (48.89)
Sibling	27 (29.35)	20 (22.22)
Son/daughter	10 (10.87)	4 (4.44)
Friend	0	2 (2.22)
Parent	12 (13.04)	14 (15.56)
Other	8 (8.70)	6 (6.67)
FPQ-K subscale Pain knowledge mean(SD)	65.29 (16.93)	64.59 (18.53)[a]
PCRS Motivation mean (SD)	78.91 (11.29)	79.41 (11.02)[b]
APCA African POS subscale mean (SD)	44.20 (18.95)	45.26 (18.55)[c]

7.3.2 Carer characteristics

The mean age of the carer participants in the two arms of the trial were similar (41.1 years in the pain education intervention and 42.6 years in the

[a] FPQ: scores range from 0-90; higher scores represents positive outcome

[b] PCRS: scores range from 0-64; higher scores represents positive outcome

[c] APCA African POS: scores range from 0-15; higher scores (with some items reversed) represents positive outcomes

usual care group) but there was a slight difference in terms of gender between the two groups. More male carers were randomised to the usual care group 19/90 compared with 14/92 in the pain education intervention group. There were also no differences with regard to marital status, education level and religion.

There were more carer participants who classed themselves as housewives in the usual care group 30/90 compared with 24/92 in the pain education intervention group. There were also baseline differences between groups in terms of the relationship of carer to patient. In the usual care group 44 of 90 carer participants were spouses to the patient compared with 35/92 in the pain education intervention group. Conversely there were more sibling

carers in the pain education intervention group 27/92 compared with 20/90 in the usual care group. There were more sons and daughters of patients among the carers in the pain education group 10/92 compared with 4/90 in the usual care group. There were no differences at baseline in the mean scores regarding carer knowledge of pain management, carer motivation in provision of care and quality of life.

In summary the two groups were broadly similar at baseline in terms of age, marital status, level of education, religion and mean outcome scores, however carer participants in the pain education group were more likely to be female and less likely to be housewives.

7.4 Uptake and adherence to the interventions

Patient and carer dyads were randomly allocated to one of the two arms of the trial once baseline assessments were conducted. All of the 182 patients

and their carers received usual care provided by staff at the hospital from which they were recruited. All of the 92 patients and their carers randomised to the pain education intervention attended the face-to-face discussion which lasted for 30 minutes and received the leaflet immediately after randomisation. Of these, 59 participants received the phone call reminder intervention at week two. Due to poor telephone network coverage some participants did not receive a phone call (n=19) but had brief face-to-face contact with KN during their visit to the clinic at week two. Of the 59 participants who received a phone call, four also had face-to-face contact with me at the clinic where I reminded them to read the leaflet and clarified any questions they had.

7.5 Follow-up

Of the 182 patient/carer dyads randomised, 157 patient/carer dyads (86.26%) and a further 10 patients (without a carer) were successfully followed-up. Of the 15 patient/carer dyads lost to follow-up, 8 were from the pain education intervention group, and 7 were from the usual care group. Of the additional 10 carers lost to follow-up, 5 were from each arm of the study.

Follow-up assessments were collected from 79 patients/carer dyads allocated to the pain education intervention group and from 78 patients/carer dyads allocated to the usual care group. Follow-up assessments were also collected from 5 patients without a carer from each group.

The reasons for being lost to follow-up were various. In the pain education intervention group eight patient/carer dyads were lost to follow-up for the following reasons: two had no transport, four patients died before follow-up assessments, one patient/carer was untraceable and another patient/carer dyad had moved away to another centre. In the usual care group a total of seven patients/carer dyads were lost to follow-up for the following reasons: four of them moved to another centre, two of them were untraceable and one patient was unwell therefore assessments could not be conducted. In each group a further five carers were lost to follow-up and the reasons were all similar; two carers from each group were too busy to accompany the patient to the hospital for follow-up assessments, and three from each group had no transport to cater for both the patient and the carer.

The reasons for loss to follow-up did not differ between the two groups except that in the intervention group four patients died, but no death was reported in the usual care group. As the intervention did not involve any invasive procedures it is unlikely that these were due to the intervention.

Of the 157 patient/carer dyads and 10 patients without a carer who completed the trial, complete data were available for all the outcomes with 100% response for all outcome scales. All outcomes were conducted at baseline and eight weeks after delivery of the intervention and transposed to a 0 to 100 scale with higher scores indicating a more 'positive' outcome; hence a participant's individual score represented a percentage of the best possible score for that outcome.

7.6 Primary outcome-average pain severity

The primary outcome measure for this trial was change in average pain severity between baseline and follow-up in the two arms of the trial measured by a sub-scale of the Brief Pain Inventory.

Both groups had an improved average pain severity at follow-up (Table 21). However those in the pain education group had a mean change of 40.95 (SD 23.78) while usual care group had a mean change of 19.27 (SD 25.27). Participants in the pain education group reported a greater improvement in severity of pain compared to those in the usual care group (mean difference 21.09, 95% confidence interval 16.56 to 25.63; P<0.001). When adjustments were made for baseline average pain severity score, recruitment centre, age, gender and medication number, the result was similar (mean difference 21.25, 95% confidence interval 16.7 to 25.8; P <0.001). Regardless of the method of analysis used, the participants in the pain education intervention group appeared to have a greater improvement in pain severity than those in the usual care group.

Table 21 Primary outcome- average pain severity on the BPI-PS for pain education and usual care groups for patient participants

Outcome	Pain education (n=84)	Usual care (n=83)	Adjusted for baseline average pain severity and recruitment centre[a]		Adjusted for baseline average pain severity, recruitment centre, age, gender and medication[b]	
			Mean difference (95% CI)	P value	Mean difference (95% CI)	P value
BPI-PS subscale						
Mean (SD) average pain severity score						
At baseline (n=182)	50.76 (24.86)	51.22 (27.1)				
At follow-up (n=167)	92.62 (8.23)	71.69 (21.18)				
Mean change (SD) from baseline	40.95 (23.78)	19.27 (25.27)	21.09 (16.56 to 25.63)	<0.001	21.25 (16.7 to 25.8)	<0.001

[a]Linear regression: controlling for baseline score, and recruitment centre.

[b]Linear regression: controlling for baseline score, recruitment centre, age, gender and medication number.

7.7 Secondary outcomes (patients)

There were three secondary outcomes for the patients: pain interference with activities of daily living, patient pain knowledge of pain management, and quality of life. Table 22 presents secondary outcomes for the patients.

7.7.1 Pain interference

Both groups experienced improved pain interference score at follow-up: mean difference 42.5 (SD 25.91) in the pain education group compared with 18.42 (SD 23.92) in the usual care group. Patient participants in the pain education group had significantly greater improvement on pain interference than the usual care group (mean difference 24.32, 95% confidence interval 19.33 to 29.32; P<0.001). When adjusted for baseline pain interference score, recruitment centre, age, gender and medication number, the result was similar (mean difference 24.5, 95% confidence interval 19.61 to 29.38; P<0.001). In both analyses patient participants in the pain education intervention had a significantly greater improvement on pain interference with daily activities than patient participants in the usual care group.

7.7.2 Pain knowledge

Both groups reported improved pain knowledge: mean difference 25.63 (SD 15.5) in the pain education group compared with 6.32 (SD 11) in the usual care group. Patients in the pain education group reported greater

improvement in knowledge than patients in the usual care group (mean difference 20.05, 95% confidence interval 17.25 to 22.86; P<0.001). When adjusted for baseline patient pain knowledge score, recruitment centre, age, gender and medication number, the result was similar (mean difference 20.39, 95% confidence interval 17.51 to 23.27; P<0.001. Patient participants in the pain education intervention group had significantly more knowledge of pain management than patient participants in the usual care group regardless of the method of analysis used.

7.7.3 Quality of life (palliative care outcomes)

At follow-up both the pain education group and the usual care group reported improved quality of life (palliative care outcomes), mean difference 45.44 (SD 22.58) in the pain education group compared with 14.46 (SD 18.77) in the usual care group. Patient participants in the pain education group experienced a better quality of life than participants in the usual care group (mean difference 28.32, 95% confidence interval 24.12 to 32.53; P<0.001). After adjustments were made for baseline quality of life score, recruitment centre, age, gender and medication number, the result was similar (mean difference 28.76, 95% confidence interval 24.62 to 32.91; P<0.001). In both analyses patient participants in the pain education intervention group had significantly a better quality of life than participants in the usual care group.

Table 22 Secondary outcomes- pain interference, pain knowledge and quality of life for patient participants

Outcome	Pain education (n=84)	Usual care (n=83)	Adjusted for baseline score and recruitment centre[a]		Adjusted for baseline score, recruitment centre, age, gender and medication number[b]	
			Mean difference (95% CI)	P value	Mean difference (95% CI)	P value
BPI-PI subscale						
Mean (SD) pain interference						
At baseline (n=182)	49.91 (27.97)	49.46 (29.48)				
At follow-up (n=167)	93.67 (9.33)	69.24 (25.21)				
Mean change (SD) from baseline	42.5 (25.91)	18.42 (23.92)	24.32 (19.33 to 29.32)	<0.001	24.5 (19.61 to 29.38)	<0.001
PPQ-K subscale Mean pain knowledge						
At baseline (n=182)	67.78 (16.61)	66.24 (18.84)				
At follow-up (n=167)	92.63 (8.16)	71.98 (15.21)				
Mean (SD) change from baseline	25.63 (15.5)	6.32 (11.00)	20.05 (17.25 to 22.86)	<0.001	20.39 (17.51 to 23.27)	<0.001
APCA African POS-patient subscale						
Mean (SD) POS						
At baseline (n=182)	44.78 (22.79)	48.92 (20.5)				
At follow-up(n=167)	90.58 (9.0)	63.37 (19.46)				
Mean (SD) change from baseline	45.44 (22.58)	14.46 (18.77)	28.32 (24.12 to 32.53)	<0.001	28.76 (24.62 to 32.91)	<0.001

[a]Linear regression: controlling for baseline score and recruitment centre

[b]Linear regression: controlling for baseline score, recruitment centre, age, gender and medication number

7.8 Carers' secondary outcomes

There were three secondary outcomes for the carers: carers' knowledge of pain management, carers' motivation to provide care and quality of life. Table 23 presents the secondary outcomes for the carers.

7.8.1 Pain knowledge

Both groups reported improved pain knowledge: mean difference 27 (SD 15.8) in the pain education group compared with 7.17 (SD 9.8) in the usual care group. Carers in the pain education group reported greater improvement in knowledge than carers in the usual care group (mean difference 20.51, 95% confidence interval 17.58 to 23.44; P<0.001). When adjusted for baseline carers' pain knowledge score, recruitment centre, age, and gender the results were similar (mean difference 20.32, 95% confidence interval 17.37 to 23.28; P<0.001). Regardless of the method of analysis, carers in the pain education intervention group had a significantly improved knowledge of pain management than carers in the usual care group.

7.8.2 Motivation

Both groups reported improved motivation to provide care: mean difference 18.01(SD 11.96) in the pain education group compared with 10.18 (SD 8.48) in the usual care group. Carers in the pain education group reported greater motivation to provide care than carers in the usual

care group (mean difference 7.7, 95% confidence interval 5.26 to 10.14; P<0.001). When adjusted for baseline carers' pain knowledge score, recruitment centre, age, and gender the results were similar (mean difference 7.74, 95% confidence interval 5.15 to 10.13; P<0.001). Carers in the pain education intervention group were more motivated to provide care than carers in the usual care group.

7.8.3 Quality of life

Both groups reported improved quality of life: mean difference 47.68 (SD 18.86) in the pain education group compared with 13.42 (SD 16.63) in the usual care group. Carers in the pain education group reported a better quality of life than carers in the usual care group (mean difference 34.13, 95% confidence interval 30.16 to 38.09; P<0.001). When adjusted for baseline carers' quality of life score, recruitment centre, age, and gender the results were similar (mean difference 34.16 95% confidence interval 30.15 to 38.17; P<0.001). Carers in the pain education intervention had a significantly better quality of life than carers in the usual care group, regardless of the method of analysis used.

Table 23 Secondary outcomes- pain knowledge, motivation and quality of life for carer participants

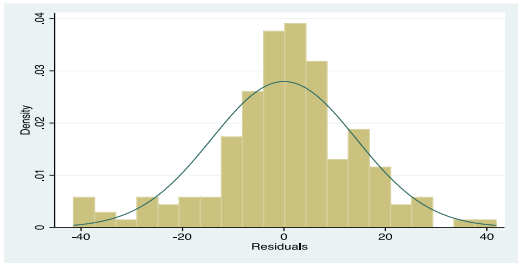
Outcome	Pain education (n=79)	Usual care (n=78)	Adjusted for baseline score and recruitment centre[a]		Adjusted for baseline score, recruitment centre, age, gender[b]	
			Mean difference (95% CI)	P value	Mean difference (95% CI)	P value
FPQ-K subscale						
Mean pain knowledge						
At baseline (n=182)	65.29 (16.93)	64.59 (18.53)				
At follow-up (n=157)	91.36 (7.8)	70.26 (15.88)				
Mean (SD) change from baseline	27 (15.8)	7.17 (9.8)	20.51 (17.58 to 23.44)	<0.001	20.32 (17.37 to 23.28)	<0.001
PCRS motivation Mean (SD)						
At baseline (n=182)	78.91 (11.29)	79.41 (11.02)				
At follow-up (n=157)	97.13 (5.87)	89.52 (11.14)				
Mean (SD) change from baseline	18.01 (11.96)	10.18 (8.48)	7.7 (5.26 to 10.14)	<0.001	7.64 (5.15 to 10.13)	<0.001
APCA African POS-carer subscale Mean (SD) POS						
At baseline (n=182)	44.2 (18.95)	45.26 (18.55)				
At follow-up (n=157)	92.66 (8.84)	58.55 (17.94)				
Mean (SD) change from baseline	47.68 (18.86)	13.42 (16.63)	34.13 (30.16 to 38.09)	<0.001	34.16 (30.15 to 38.17)	<0.001

[a] Linear regression: controlling for baseline score and recruitment centre.

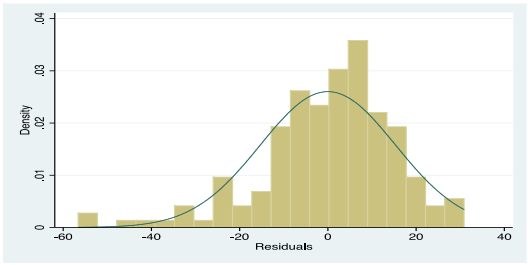
[b] Linear regression: controlling for baseline score, recruitment centre, age and gender.

7.9 Assumptions of regression analysis

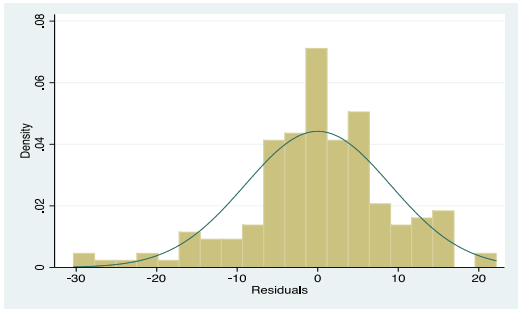
Figure 14: Histograms of residuals for each fully adjusted model for patient outcomes



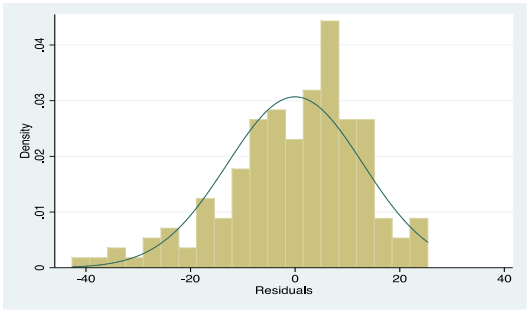
BPI-PS subscale[a]



BPI-PI subscale[b]



PPQ-K subscale pain knowledge[c]



APCA African POS-patient subscale[d]

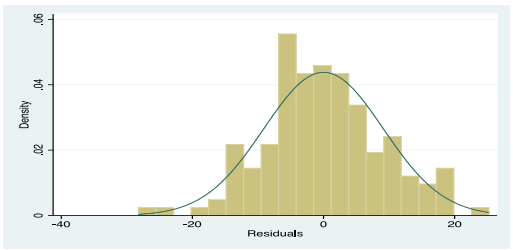
[a] BPI-PS: Brief pain inventory pain severity

[b] BPI-PI: Brief pain inventory pain interference

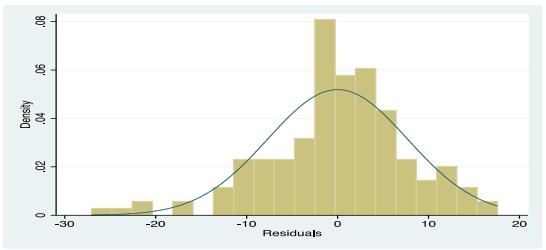
[c] PPQ-K: patient pain questionnaire-knowledge subscale

[d] APCA African POS: Palliative care outcomes-patient subscale

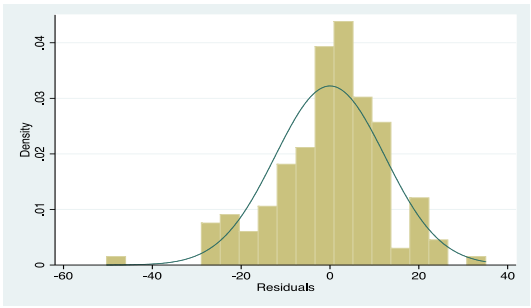
Figure 15: Histograms of residuals for each fully adjusted model for family carers outcomes



FPQ-K subscale[a]



PCRS motivation[b]



APCA African POS-carer subscale[c]

Figures 14 and 15 show the distribution of the residuals (actual values minus fitted values using fully adjusted models). While there is some evidence of left skew in the BPI-PI subscale and APCA African POS-patient subscale models, none appeared to be sufficiently non-normally distributed to suggest the model assumptions were violated.

---

[a] FPQ-K: Family pain questionnaire-Knowledge subscale

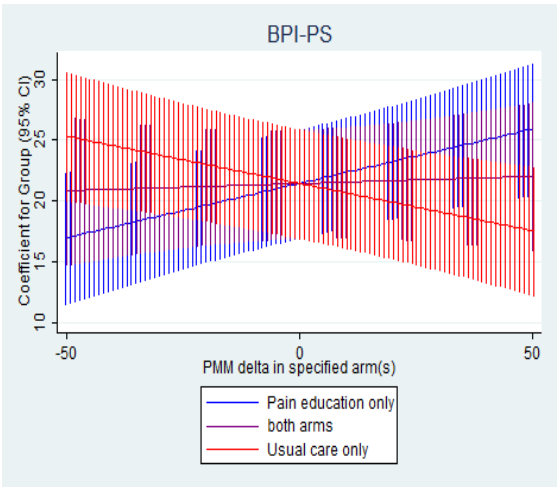
[b] PCRS: Picot caregivers rewards scale

[c] APCA African POS: palliative care outcomes-carer subscale

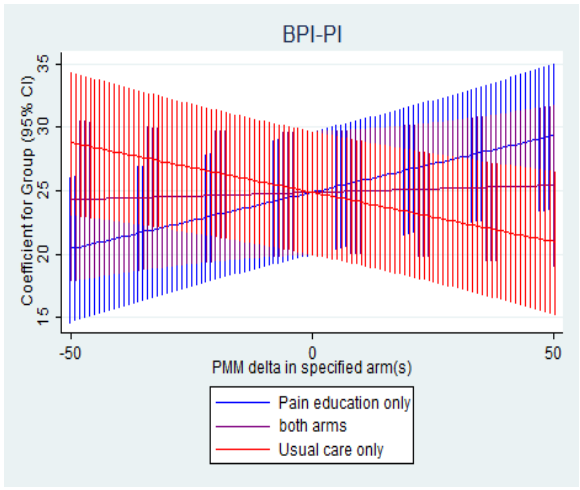
7.10 Sensitivity analysis

In sensitivity analysis for each of the seven outcomes, three scenarios were tested: (1) a difference of plus or minus 50 points for both arms (2) a difference of plus or minus 50 points for the pain education group and (3) a difference of plus or minus 50 points for the usual care group. For the first scenario this assumes that those lost to follow-up differ to those not lost to follow-up but that that this difference is consistent between trial arms. For the second scenario the assumption is that differences between those followed up and those lost to follow-up is restricted to the pain education group. In the third scenario the assumption is that differences between those followed up and those lost to follow-up is restricted to the usual care group. Figure 16 and Figure 17 summarises the results of sensitivity analysis and can be understood as follows. At zero on each axis, the estimated differences is that reported on the basis of no differences in those lost to follow-up from the fully adjusted models reported in tables 21,22 and 23. The 'whiskers' represent 95% confidence intervals. More extreme assumptions can be found with departures from zero along each x axis. Departures towards the left-hand side assume those lost to follow-up have worse outcomes, and to the right, better outcomes. For all of these scenarios and for all outcomes the 95% confidence intervals do not include zero on the y axis. In each scenario tested using various departures from the missing at random assumption, none altered the interpretation of better outcomes for the pain education group.

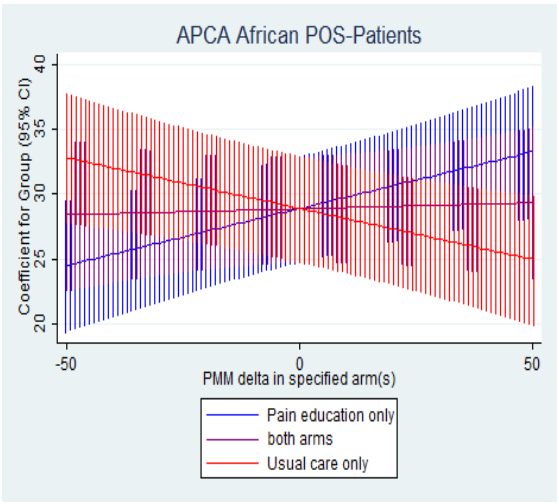
Figure 16: Sensitivity analysis for patient outcomes



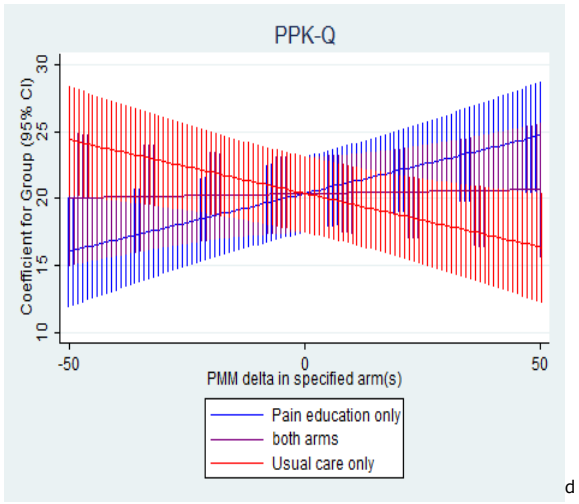
a



b



c



d

---

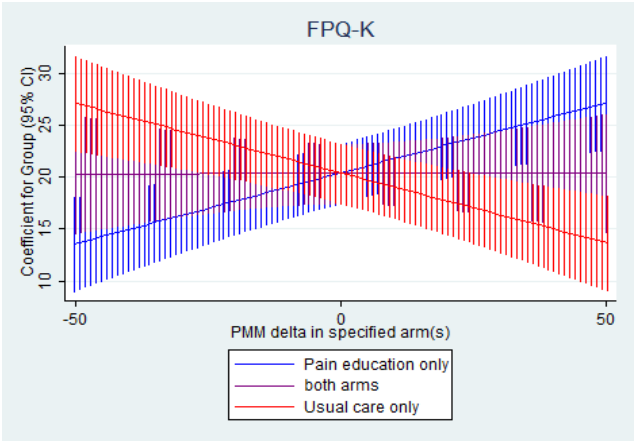
[a] BPI-PS: Brief pain inventory average pain severity

[b] BPI-PI:Brief pain inventory pain interference

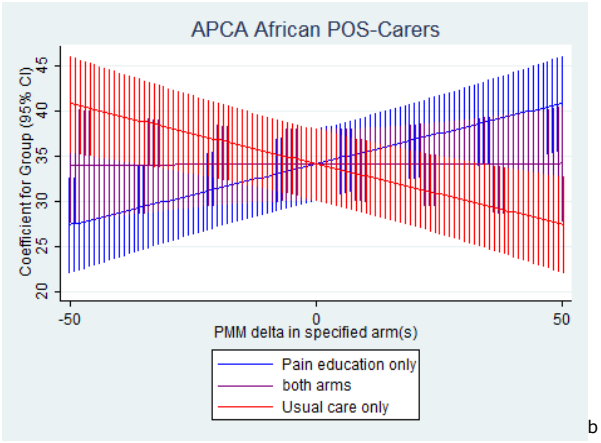
[c] APCA African POS: Palliative care outcomes; patient subscale

[d] PPK-Q: Patient pain knowledge questionnaire

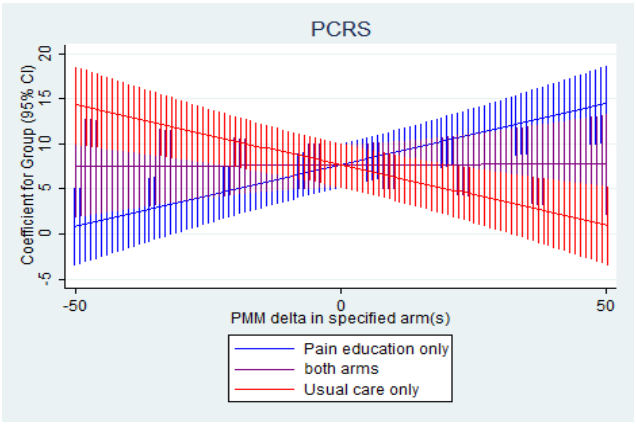
Figure 17: Sensitivity analysis of carer outcomes



a



b



c

[a] FPQ-K Family pain questionnaire; care knowledge of pain management

[b] APCA African POS carers: Palliative care outcomes; carers subscale

[c] PCRS: Picot caregiver rewards scale; carers motivation to provide care

7.11 Pain description and location

At follow-up, of the 92 patients randomised to the pain education group, 76 patients (82.6%) had pain. At follow-up of the 90 patients randomised to the usual care group, 72 patients (80%) had pain.

The most prevalent pain at follow-up was chest/abdominal pains (44.57%), limb/joint pains (31.52%) and general body pains (27.17%), in the pain education group compared with chest/abdominal pains (36.67%), general body pains (28.89%) and limb/joint pains in the usual care group (27.78%).

The prevalence of back pain, head/neck pain and mouth sores was low in both groups at follow-up. In the pain education group the prevalence of back pain was 4.35%, head/neck pain was 2.17% and mouth sores was 1.09%. In the usual care group the prevalence of back pain was 7.78%, head/neck pain was 2.22% and mouth sores was 2.22%. Table 24 summarises the description, location and prevalence of pain symptoms in both groups at baseline and follow-up.

Table 24 Pain description and location

	Pain education (N=92)		Usual care (N=90)	
Pain description and location	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**
No pain	N=2 (2.17%)	N=16 (17.39%)	N=6 (6.66%)	N=18 (20%)
Complained of pain	N=90 (97.8%)	N=76 (82.6%)	N=84 (93.3%)	N=72 (80%)
General body pain	N=18(19.57%)	N=25 (27.17%)	N=15 (16.67%)	N=26 (28.89%)
Head and neck	N=16(17.39%)	N= 2 (2.17%)	N=20 (22.22%)	N= 2 (2.22%)
Mouth sores	N= 3 (3.26%)	N= 1 (1.09%)	N= 3 (3.33%)	N= 2 (2.22%)
Limb and joint pain	N=28(30.43%)	N=29 (31.52%)	N=24 (26.67%)	N= 25(27.78%)
Chest & abdominal pain	N=41(44.57%)	N=41 (44.57%)	N=33 (36.67%)	N= 33(36.67%)
Back pain	N= 7 (7.61%)	N= 4 (4.35%)	N= 9 (10%)	N= 7 (7.78%)

7.12 Analgesia for treatment of pain

The odds ratio of the patient participant in the pain education group for being on analgesia for treatment of pain at follow-up was 1.57 times (95% confidence interval 0.66 to 3.76; P=0.31) less than the odds ratio in the usual care group, after adjusting for pain medication at baseline and recruitment centre. The odds ratio of the patient participant in the pain education group for being on analgesia for treatment of pain was 1.48 times less (95% confidence interval 0.61 to 3.59; P=0.39) than the odds ratio in the usual care group, after adjusting for baseline pain medication, recruitment centre, age and gender. Table 25 summarises both adjusted and unadjusted analyses. There was no difference between the pain education group and the usual care group in both analyses on whether the patient was on analgesia for treatment of pain or no analgesia.

Table 25 Analgesia for treatment of pain

	Pain education (N=92)		Usual care (N=90)		Unadjusted OR 95% CI[a]	P value	Adjusted OR 95% CI[b]	P value
Analgesia for pain	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**				
Yes	N=85 (92.4%)	N=82 (89%)	N=79 (87.8%)	N=75 (83.3%)				
No	N=7 (7.6%)	N=10 (11%)	N=11 (12.2%)	N=15 (16.7%)	1.57 (0.66 to 3.76)	0.31	1.48 (0.61 to 3.59)	0.39

[a]Logistic regression: controlling for baseline medication, and recruitment centre

[b] Logistic regression: controlling for baseline medication, recruitment centre, age and gender.

7.13 Type of pain medication/analgesia for treatment of pain

The odds ratio of the patient participant in the pain education group for receiving Brufen at follow-up was 0.59 (95% confidence interval 0.31 to 1.11; P=0.10) times less than the odds ratio in the usual care group.

The odds ratio of the patient participant in the pain education group for receiving Codeine at follow-up was 6.18 (95% confidence interval 1.99 to 19.14; P=0.002) times greater than the odds ratio in the usual care group.

The odds ratio of the patient participant in the pain education group for receiving Diclofenac at follow-up was 5.21 (95% confidence interval 1.86 to 14.56; P<0.001) times greater than the odds in the usual care group.

The odds ratio of the patient participant in the pain education group for receiving Panadol at follow-up was 0.54 times (95% confidence interval 0.28 to 1.04; P=0.06) less than the odds ratio in the usual care group. Table 26 summarises the type of medication received.

Table 26 Type of medication received

	Pain education (N=92)		Usual care group (N=90)		OR 95% CI[a]	P value
Type of medication	**Baseline**	**Follow-up**	**Baseline**	**Follow-up**		
Amitriptyline	N=2(2.17%)	N=3(3.26%)	N=1(1.11%)	N=0	Not estimated	
Aspirin	N=1(1.09%)	N=0	N=2(2.22%)	N=2(2.22%)	Not estimated	
Brufen	N=6(6.52%)	N=30(32.6%)	N=7(7.78%)	N=38(42.2%)	0.59 (0.31 to 1.11)	0.10
Codeine	N=3(3.26%)	N=23(25%)	N=1(1.11%)	N=5(5.56%)	6.18 (1.99 to 19.14)	0.002
Diclofenac	N=5(5.43%)	27(29.35%)	N=5(5.56%)	10 (11.11%)	5.21 (1.86 to 14.56)	<0.001
Indocid	N=1(1.09%)	N=1(1.09%)	N=1(1.11%)	N=1(1.11%)	Not estimated	
Panadol	N=79(85.9%)	N=44(47.8%)	N=70(77.8%)	N=52(57.8%)	0.54 (0.28 to 1.04)	0.06
Any analgesia	N=85(92.4%)	N=82(89%)	N=79(87.8%)	N=75(83.3%)	1.48 (0.61 to 3.59)	0.39

[a]Logistic regression: controlling for type of medication at baseline, recruitment centre, patient age and gender.

7.14 Association of baseline factors with outcomes

An improvement on average pain severity was associated with lower age of the patient (regression coefficient -0.28, 95% confidence interval -0.48 to -0.08; P=0.006). For every one year increase in age, there was an average worsening in pain severity score of 0.28 points. There was no evidence that change in pain severity was associated with gender (mean difference -3.70, 95% confidence interval -8.31 to 0.91; P=0.12, recruitment centre (mean difference 2.1, 95% confidence interval -2.70 to 7.07; P=0.38) and number of medications (mean difference -1.16, 95% confidence interval -6.27 to 3.95; P=0.65).

Change in pain interference score was associated with the age of the patient (regression coefficient -0.37, 95% confidence interval -0.59 to -0.16; P=0.001). For every one year increase in age there was an average worsening in pain interference score of 0.37 points. Change in pain interference was also associated with gender of the patient. Females experienced a significant less improvement in pain interference compared to males (mean difference -5.57, 95% confidence interval -10.52 to -0.61; P=0.028). The mean improvement in pain interference was lower in females with an average score of 5.57 points compared to males after adjusting for other factors. There was no evidence that change in pain interference was associated with recruitment centre (mean difference -2.07, 95% confidence interval -7.02 to 2.88; P=0.41) and number of medications (mean difference -1.26, 95% confidence interval -6.53 to 4.01; P=0.64).

Patient pain knowledge of pain management was not associated with age (regression coefficient -0.07, 95% confidence interval -0.20 to 0.05; P=0.25), gender (mean difference -1.98, 95% confidence interval -4.92 to 0.96; P=0.19), recruitment centre (mean difference 2.42, 95% confidence interval -0.53 to 5.37; P=0.11) and number of medications (mean difference -0.87, 95% confidence interval -3.95 to 2.22; P=0.58).

Quality of life was associated with the age of the patient (regression coefficient -0.29, 95% confidence interval -0.47 to -0.11; P=0.002). For every one year increase in age there was an average decrease in quality of life score of 0.29 points. There was also borderline statistical significance of quality of life in relation to gender of the patient. Females experienced a statistically significant worse quality of life compared to males (mean

difference -4.21, 95% confidence interval -8.40 to -0.01; P=0.049). The mean change in quality of life was lower in females compared to males with an average score of 4.21 points after adjusting for other factors. There was no evidence that quality of life was associated with recruitment centre (mean difference 2.53, 95% confidence interval -1.67 to 6.72; P=0.24) and number of medications (mean difference -3.42, 95% confidence interval -7.88 to 1.04; P=0.13).

For carer participants knowledge of pain management was not associated with age (regression coefficient -0.13, 95% confidence interval -0.26 to 0.00; P=0.054), gender (mean difference 0.06, 95% confidence interval -3.70 to 3.83; P=0.97) and recruitment centre (mean difference -0.17, 95% confidence interval -3.17 to 2.82; P=0.91).

Carer motivation to provide care was not associated with age (regression coefficient -0.05, 95% confidence interval -0.16 to 0.06; P=0.40), gender (mean difference 0.09, 95% confidence interval -3.09 to 3.27; P=0.96) and recruitment centre (mean difference 0.24, 95% confidence interval -2.31 to 2.79; P=0.85).

For carer participants quality of life was not associated with age (regression coefficient -0.14, 95% confidence interval -0.32 to 0.04; P=0.12), gender (mean difference -1.79, 95% confidence interval -6.91 to 3.34; P=0.49) and recruitment centre (mean difference -1.79, 95% confidence interval -5.83 to 2.24; P=0.38). Table 27 summarises associating baseline factors with the outcomes.

Table 27 Association of baseline factors with outcomes

Outcome	**Adjusted for baseline score, age, gender ,recruitment centre, and medication number [a]**		
Patient participants	Associating factor	Regression coefficient (95% CI)	P value
Average pain severity (BPI-PS)	Age of patient	-0.28 (-0.48 to -0.08)	0.006
	Women vs Men	-3.70 (-8.31 to 0.91)	0.12
	Recruitment centre	2.19 (-2.70 to 7.07)	0.38
	Medication number	-1.16 (-6.27 to 3.95)	0.65
Pain interference (BPI-PI)	Age of patient	-0.37 (-0.59 to -0.16)	0.001
	Women vs Men	-5.57 (-10.52 to -0.61)	0.028
	Recruitment centre	-2.07 (-7.02 to 2.88)	0.41
	Medication number	-1.26 (-6.53 to 4.01)	0.64
Pain knowledge (PPQ-K)	Age of patient	-0.07 (-0.19 to 0.05)	0.25
	Women vs Men	-1.98 (-4.92 to 0.96)	0.19
	Recruitment centre	2.42 (-0.53 to 5.37)	0.11
	Medication number	-0.87 (-3.95 to 2.22)	0.58
Quality of life (APCA African POS)	Age of patient	-0.29 (-.47 to -.11)	0.002
	Women vs Men	-4.2 (-8.4 to -.01)	0.049
	Recruitment centre	2.53 (-1.67 to 6.72)	0.24
	Medication number	-3.42 (-7.88 to 1.04)	0.13
Carer participants	**Adjusted for baseline score, age, gender, and recruitment centre [b]**		
Pain knowledge (FPQ-PK)	Age of carer	-0.13 (-0.26 to 0.002)	0.054
	Women vs Men	0.06 (-3.70 to 3.83)	0.97
	Recruitment centre	-0.17 (-3.17 to 2.82)	0.91
Motivation (PCRS)	Age of carer	-0.05 (-0.16 to 0.06)	0.40
	Women vs Men	0.09 (-3.09 to 3.27)	0.96
	Recruitment centre	0.24 (-2.31 to 2.79)	0.85
Quality of life (APCA African POS)	Age of carer	-0.14 (-0.32 to 0.04)	0.12
	Women vs Men	-1.79 (-6.91 to 3.34)	0.49
	Recruitment centre	-1.79 (-5.83 to 2.24)	0.38

[a]Linear regression: controlling for baseline score, age, gender, recruitment centre and number of medication.

[b] Linear regression: controlling for baseline score, age, gender and recruitment centre.

7.15 Summary

Of the 182 participants (patient/carer dyads), 92 were randomised to pain education intervention and 90 received usual care. Of these 157 patient/carer dyads and 10 patients completed all outcome measurers. Based on the analyses of these available data, patients in both the pain

education intervention group and the usual care group had reduced pain severity, reduced pain interference with daily activities, improved pain knowledge and a better quality of life. Likewise carer participants in both groups had improved knowledge of pain management, more motivated to provide care and a better quality of life, however participants (patient/carer dyads) in the pain education intervention had less severity of pain, less pain interference, more knowledge of pain management, more motivated to provide care and a better quality of life outcomes than participants in the usual care group. In the next chapter, the results of the pain education trial and the design of the pain education study are discussed.

CHAPTER EIGHT: DISCUSSION

8.1 Introduction

The aim of this study was to test the effects of a pain educational intervention on pain severity among people living with HIV/AIDS in Malawi. The secondary aims were to: (1) investigate if the pain education intervention reduces pain interference with daily activities, improves knowledge of pain management and improves quality of life among people living with HIV/AIDS; and (2) investigate if the pain education intervention improves knowledge of pain management, improves quality of life, and improves motivation to provide care among family carers of patients with HIV/AIDS. In this chapter, the results and methodological strengths and limitations of the study are discussed. The findings are discussed in the context of other studies of pain management in HIV/AIDS, cancer and other related chronic conditions. In this chapter I highlight the original contribution this study makes to the field of pain management in HIV/AIDS. The implications of the study findings for the care of people living with HIV/AIDS in Malawi is discussed.

8.2 Overview of the main study findings

The findings from this study suggest that the pain education intervention which took the form of an information leaflet, face-to-face discussion and a follow-up phone call at two weeks had positive effects on both the physical and psychological health of people living with HIV/AIDS and their family

carers. Patient participants randomised to the pain education intervention experienced a greater reduction in pain severity, pain interference with general activities, greater knowledge of pain management and a better quality of life compared to participants randomised to the usual care group. Carer participants randomised to the pain education intervention group reported a greater knowledge of pain management, greater motivation to provide care and a better quality of life compared to participants in the usual care group.

8.3 Effectiveness of the pain education intervention

Complex interventions are unlikely to have a simple and linear cause-effect relationship with any outcome because they have multiple interacting components. It is difficult to know if the components work individually or together (Petticrew, 2011). Without testing the individual components individually (and thereby losing the combined effect) it is not possible to determine which elements trigger the responses observed. If the pain education intervention is adopted into routine care it's important to develop an effective monitoring mechanism in order to detect long term outcomes that could not be observed through the original study (Craig et al., 2008).

The pain education intervention was guided by the bio-psychosocial model. The contents and individual components of the intervention focused on biological, psychological, and social needs. These are the needs that patients with HIV/AIDS have frequently reported as not being properly addressed. The medical research council framework for development and evaluating complex

interventions supports the notion of a theory-based intervention in order to understand how change in outcomes occur between the two groups (Craig et al., 2008). The presence of the family carer as study participants is likely to have strengthened the intervention.

Another way to understand how the pain education intervention 'worked' is by identifying the techniques, procedures and processes used to generate the intervention (Michie and Abraham, 2004). The pain education intervention was also underpinned by the adult learner's theory. The face-to-face discussion ensured active participation of study participants which potentially enabled them to discuss their pain freely. However the current design of the study does not explain the exact mechanism by which the pain education intervention worked. This is partly due to absence of qualitative data to support the positive benefits observed in the study.

8.4 Strengths and limitations of the study

8.4.1 Study design

The randomised controlled trial is the gold standard of evaluating the effect of any intervention among patients and family carers of people living with HIV/AIDS. To my knowledge this is the first randomised controlled trial to investigate the effect of a nurse-led pain education intervention among people living with HIV/AIDS and their family carers in Malawi. Previous randomised controlled trials among HIV/AIDS patients have been conducted exclusively

(Goujard et al., 2003, Wu et al., 2006, Gifford et al., 1998) or predominantly (Wantland et al., 2008) in western countries. None of these trials recruited patient/care dyads as participants in their studies. The only study which recruited patient/carer dyads was conducted in Australia and had a small sample size (n=36) (Pakenham et al., 2002). In the Australian study, the focus was on the emotional and social problems faced by carers using psychological counselling.

The sample size of 182 in the current study is larger than other trials conducted in USA (Gifford et al., 1998, Webel, 2010) and Taiwan (Chiou et al., 2006a). Other larger randomised controlled trials were either conducted in France (Goujard et al., 2003) or were multinational and had many recruitment sites in the USA, with a few sites in South Africa (Wantland et al., 2008). However I did not power secondary outcomes.

The current study was conducted in two public hospitals in the northern part of Malawi where protocols for usual care were broadly similar at the time the study was being conducted. However environmental factors such as attitude of staff members and hospital layout may have differed between the two hospitals. The study was not large enough to formally test this either through sub-group analysis or testing for an interaction effect between hospital and intervention.

Inclusion criteria were restricted to those with CD4 count <350 cells or stages III/IV of HIV infection. This is the crucial stage in HIV infection because patients are likely to be in pain due to opportunistic infections (Solano et al,

2006) and side effects of HIV treatment (Wadley et al, 2011). At both recruitment sites CD4 count is tested, but there is a charge to patients of around £5 for laboratory services. Many people are poor in Malawi and not able to pay for laboratory services and therefore clinicians have to rely on HIV clinical staging. A recent systematic review has reported that WHO clinical staging misses a high proportion of individuals who are eligible to start HAART based on CD4 count (Munthali et al., 2014) suggesting that identifying individuals likely to benefit from this intervention does not need to rely on costly laboratory tests.

The pilot study was relatively small and therefore a larger pilot study may have thrown up other design issues for the current study.

8.4.2 Recruitment and follow-up

In spite of the process of recruiting patient/carer dyads who met the criteria for this study being challenging, recruitment targets were met. It was emphasised to participants that involvement in the study was voluntary. Participants were recruited through the HIV/AIDS clinics either during the registration to start HIV treatment or during their routine follow-up to the HIV/AIDS and palliative care clinics. Participants had between two and four weeks to discuss with their family members the possibility of taking part in the study. By being involved in some tasks and activities at the clinics such as checking weight and height and registration of patients I managed to build some rapport with potential study participants. Staff in the HIV/AIDS clinics

were involved in giving explanations about the study and information sheets and were encouraging without being coercive.

Attrition for the study was 8 % (15/182) and 14% (25/182) for patients and carers respectively. This is low compared to other studies that have reported up to 34.6% attrition (Wantland et al., 2008) and 35% attrition (Lovell et al., 2010). In the current study, the reasons for patient/carer dyads loss to follow-up being death of the patient, a lack of transport money, having moved away, being untraceable and the patient being too unwell. The reasons for carers' loss to follow-up were lack of transport to accompany the patient to the clinic and being too busy.

There were eight patient/carer dyads lost to follow-up in the intervention arm and seven patient/carer dyads lost to follow-up in the usual care arm. There were five carers in each arm who were lost to follow-up. The reasons for loss to follow-up did not differ apart from in one respect. There were four patients who were lost to follow-up due to death and all were randomised to the pain education intervention. I did not have access to their records to look at the causes of death but the nature of the intervention meant it was unlikely to have been related.

Follow-up assessments were conducted once, at week eight after randomisation and delivery of the intervention. This was judged to be sufficient time to observe the effects of the intervention and is consistent with other pain education studies (Clotfelter, 1999, Hudson et al., 2005) and based on recommendation from pain research experts (Bennett and Closs, 2011).

However, it is not possible to infer from the present study whether the observed effects would persist beyond eight weeks period due to the limitations on time and resources for further follow-up assessments.

A range of secondary outcomes were chosen due to the complex nature of the intervention (Bennett and Closs, 2011). Patient outcomes are in line with IMMPACT (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials) recommendation on core outcomes for patients with chronic pain (Dworkin et al., 2008, Dworkin et al., 2005b, Turk et al., 2003). In one study of a pain education intervention (Wantland et al., 2008) outcomes were conducted at two time points (at one month and two month after delivery of the intervention and results were statistically significant at one month and were maintained at two month follow-up. In another study (Goujard et al., 2003) outcomes were assessed at six months and the findings were statistically significant for all but one outcome and this was maintained at 12 and 18 months. In another study of coping strategies among men with HIV/AIDS (Chesney et al., 2003) follow-up assessments were conducted at three, six and 12 months post intervention. The results were statistically significant at three months, but at six and 12 months significant differences were maintained for only one outcome. In a randomised controlled trial among dementia patients and their family carers (Graff et al., 2006), they conducted outcomes at week six and week 12 after delivery of the intervention, the results were statistically different for all outcomes at week six and were maintained at week 12. From these studies it is difficult to infer that educational interventions have longer lasting effects for HIV/AIDS patients.

8.4.3 Randomisation, blinding and contamination

Randomisation was prepared by my supervisor (AA) in the UK using a computerised random binary series and block randomisation to ensure that there was no great imbalance between the two groups. Randomisation appeared to be successful because the number of patients and carer participants and their characteristics were broadly similar at baseline. I implemented randomisation using opaque sealed and consecutively numbered envelopes. I was not involved in the preparation of the envelopes and I did not know the block size until after I finished data collection and returned to the UK for data analysis. This prevented me from predicting the allocation in advance.

In this study participants knew to which group they were allocated due to the nature of the study. It was not possible to blind study participants. This has potential for performance bias. As I also knew the group each participant was allocated to, and to minimise assessment bias, I conducted baseline assessments before randomisation. Nurses' blind to treatment allocation conducted follow-up assessments. However performance bias cannot be excluded because of the fact that some pain education group participants had developed a good working relationship with me through a series of verbal interactions. Moreover patient reported outcomes such as pain intensity are subjective (Bennett and Closs, 2011) and in this study all the outcomes were self-reported by patients and family carers. A double-blinded trial, although

methodologically superior was not possible in a study of a non-pharmacological intervention of this type (Bennett and Closs, 2011).

Contamination between the two arms of the trial cannot be excluded because study participants lived in the same community and some were neighbours or friends. To minimise this, participants who were allocated to the pain education intervention were asked not to share the leaflet with their friends and not to report the face-to-face discussion they had with me. The leaflet was put in an envelope and participants were asked to keep it safe before they left the room where the intervention was delivered. Participants were further asked not to speak to healthcare staff about the intervention. As participants lived in communities where they would inevitably interact with their friends and neighbours with similar problems, I cannot exclude the possibility of contamination between groups. Nurses and other health care workers who were involved in the development of the intervention (information leaflet) were informed not to share the information leaflet with the patients during clinical appointments. However it is difficult to know if they did not share the information leaflet with the patients because I was not present during clinical appointments.

Clustering the participants and randomising according to some natural grouping such as area or clinic could have avoided contamination thereby reducing type II error (Torgerson, 2001), but this was not possible for various reasons. Cluster randomisation requires larger sample sizes, and sufficient number of clusters, more complex design and analysis (Sedgwick, 2012) outside of the scope of a doctoral study.

A crossover design is another alternative to overcome contamination, where participants act as their own controls. This also reduces placebo effects, and requires smaller sample sizes than parallel design. However cross over design take longer and would have been a challenge in this study where HIV/AIDS patients undergo natural fluctuations in their condition such that symptoms may be better or worse when participants are in a different arm (i.e. treatment order) of the trial (Bennett and Closs, 2011). HIV/AIDS is associated with comorbidities such as cancer (Yeguez et al., 2003, Matheny, 2001), and liver disease (Rabinstein, 2003) and their health can change at any time. Participants can easily drop out (Bennett and Closs, 2011), or even transfer to other centres for their own reasons. Crossover trials are problematic where there are carry over effects (Mills et al., 2009). Although a wash out period (no treatment) before crossing to the other arm helps to minimise carry over effects (Sibbald and Roberts, 1998), it would have been impossible to reverse the effects of an educational intervention after being delivered in the experiment arm before crossing to a control arm.

8.4.4 Data analysis

Data was analysed blind to treatment groups to minimise bias using intention-to-treat analysis. This is the most robust method of data analysis in clinical trials. Intention-to-treat is a strategy for the analysis of randomised controlled trials that compares participants in the groups to that which they were originally randomly assigned (Hollis and Campbell, 1999, Sedgwick, 2011),

promoting internal validity (Sedgwick, 2013). I utilised a modified intention-to-treat analysis strategy, where participants lost to follow-up were all excluded from the analysis because it is only possible to apply a strict intention-to-treat analysis where there is no attrition (Hollis and Campbell, 1999, Abraha and Montedori, 2010).

Per protocol analysis was not applicable in this study because no participant deviated from the treatment randomly allocated to receive treatment to which they were not randomised (Montori and Guyatt, 2001, Sedgwick, 2013, Sedgwick, 2011). Therefore in this study it is unlikely that there was underestimation of the magnitude effect of the treatment because there was no problem of adherence that I was aware of (Montori and Guyatt, 2001) or an overestimation of the clinical effectiveness due to loss to follow-up (Hollis and Campbell, 1999). Findings of the study were robust to the sensitivity analysis conducted.

The pain education intervention study was delivered by myself, a nurse who has studied to master's level in palliative and end-of-life care. This meant that the intervention was grounded in the existing literature and built on five years of experience in this area. However it is also a limitation because of the problem of reproducibility. In Malawi, we have few nurses trained in palliative care up to Masters Level. An important question remains as to the level of skill required to deliver this intervention effectively.

8.5 Comparison with other studies

The pain education intervention should be considered as a complex intervention because it is built up from a number of various components acting both interdependently and independently (Craig et al., 2008, Bennett and Closs, 2011). The Medical Research Council framework for complex interventions was designed for the development, implementation and evaluation of randomised controlled trials to improve health care services (Craig et al., 2008). Designing and developing the pain education intervention was challenging. It needed a substantial amount of time and effort. However in this trial few participants declined to take part in the study and attrition was also low suggesting that the intervention is feasible and acceptable among patients with HIV/AIDS and their family carers. It is challenging to compare the results of this study with other studies because most of the pain education studies have been conducted in western countries and have produced conflicting results. Few studies in the field of HIV/AIDS focussing on pain education have been conducted in sub-Saharan Africa. The interventions in other studies have also been highly variable and often poorly described. A systematic review (Millard et al., 2013) concluded that randomised controlled trials of self-management programmes for people living with HIV/AIDS result in short-term improvements in physical, psychological, social, health knowledge and behavioural outcomes. This review retained eight randomised controlled trials, six studies were conducted in the USA and two studies were conducted in Taiwan.

Table 28 below summaries a comparison of previous intervention studies conducted in the field of HIV/AIDS, cancer and other chronic illnesses with the current study. In the text that follow this table, I compare the findings of the present study with other work in terms of the seven outcome measures.

Table 28 Comparison of the findings from the current study with previous work

Studies and sample	Outcomes from the current study						
	Patient pain severity	**Patient pain interference**	**Patient pain knowledge**	**Patient quality of life**	**Carer pain knowledge**	**Carer motivation**	**Carer quality of life**
Nkhoma (2014) (n=182)	✓	✓	✓	✓	✓	✓	✓
Catz and Balderson et al (2014) (n=452)	N/A	N/A	N/A	✓	N/A	N/A	N/A
Dowse et al (2014) (n=116)	N/A	N/A	✓	N/A	N/A	N/A	N/A
Henriksson et al (2013) (n=125)	N/A	N/A	N/A	N/A	✓	✓	×
Rajesh et al (2013) (n=256)	N/A	N/A	✓	N/A	N/A	N/A	N/A
Peltzer et al (2012) (152)	N/A	N/A	✓	N/A	N/A	N/A	N/A
Smith Fawzi et al (2012) (n=130)	N/A	N/A	N/A	N/A	N/A	N/A	✓
Oldenmenger et al (2011) (n=73)	✓	✓	N/A	N/A	N/A	N/A	N/A
Lovell (2010) (n=217)	✓	×	✓	×	N/A	N/A	N/A
Wang et al (2010) (n=116)	N/A	N/A	N/A	✓	N/A	N/A	N/A
Webel (2010) (n=89)	×	N/A	N/A`	×	N/A	N/A	N/A
Bennet et al (2009) (n=3501)	✓	×	✓	N/A	N/A	N/A	N/A
Ward et al (2009) (n=161)	×	×	N/A	×	N/A	N/A	N/A
Yildirim et al (2009) (n=40)	✓	N/A	N/A	N/A	N/A	N/A	N/A
Hudson et al (2009, 2008) (n=156; n=74)	N/A	N/A	N/A	N/A	N/A	✓	✓
Boon et al (2009) (n=202)	N/A	N/A	N/A	N/A	✓	N/A	N/A
Victor et al (2009) (sample not given)	N/A	N/A	N/A	N/A	✓	✓	✓
Wantland et al (2008) (n=775)	✓	N/A	N/A	N/A	N/A	N/A	N/A
Ward et al (2008) (n=176)	×	×	N/A	×	N/A	N/A	N/A
Lin et al (2006) (n=61 dyads)	✓	✓	N/A	N/A	N/A	N/A	N/A
Chio et al (2006) (n=67)	N/A	N/A	N/A	✓	N/A	N/A	N/A
Hudson et al (2005) (n=106)	N/A	N/A	N/A	N/A	N/A	✓	×
Chiou et al (2004)	N/A	N/A	✓	N/A	N/A	N/A	N/A

(n=67)							
Studies and sample	**Outcomes from the current study**						
	Patient pain severity	**Patient pain interference**	**Patient pain knowledge**	**Patient quality of life**	**Carer pain knowledge**	**Carer motivation**	**Carer quality of life**
Miaskowski et al (2004) (n=174)	✓	N/A	N/A	N/A	N/A	N/A	N/A
Lai et al (2004) (n=30)	✓	×	N/A	N/A	N/A	N/A	N/A
Yates et al (2004) (n=189)	×	N/A	✓	×	N/A	N/A	N/A
Gordon-Garofalo and Rubin (2004) (n=28)	N/A	N/A	N/A	N/A	N/A	N/A	×
Anderson et al (2004) (n=97)	×	×	N/A	×	N/A	N/A	N/A
Goujard et al (2003) (n=367)	N/A	N/A	✓	×	N/A	N/A	N/A
Wells et al (2003) (n=64 dyads)	×	×	✓	N/A	✓	N/A	N/A
Lechner et al (2003) (n=330)	N/A	N/A	N/A	✓	N/A	N/A	N/A
Pakenham et al (2002) (n=36 dyads)	N/A	N/A	N/A	✓	✓	N/A	✓
Rotheram-Borus et al (2001) (n=307)	N/A	N/A	N/A	N/A	N/A	N/A	✓
Inouye et al (2000) (n=40)	N/A	N/A	N/A	✓	N/A	N/A	N/A
Ward et al (2000) (n=43)	×	×	N/A	×	N/A	N/A	N/A
Hensell et al (1999) (n=70)	N/A	N/A	N/A	N/A	N/A	N/A	×
Clotfelter (1999) (n=36)	✓	N/A	N/A	N/A	N/A	N/A	N/A
Gifford et al (1998) (n=71)	×	N/A	×	×	N/A	N/A	N/A
de Wit et al (1997) (n=313)	✓	N/A	✓	✓	N/A	N/A	N/A
Pomeroy et al (1995) (n=33)	N/A	N/A	N/A	N/A	N/A	N/A	✓

✓: Results similar to the current study

×: results contrary to the current study

N/A: Not applicable/ outcome not assessed

Dyads: study recruited both patients and carers

8.5.1 Effect of the pain education intervention on patient pain severity

Participants randomised to the pain education intervention reported a greater reduction in pain severity (mean difference 21.25 percentage points) compared to participants randomised to the usual care group after adjusting for baseline differences. The pain education intervention appeared to have benefitted the patients randomised to the intervention arm of the trial. This is consistent with a large trial which recruited participants from 12 sites in the USA and a few sites in Puerto Rico and Africa (Wantland et al., 2008). The study concluded that a symptom management manual reduced the frequency and intensity of HIV/AIDS symptoms compared to a nutrition management manual. There was high attrition in this latter study (34.6%) although no identified differences between those lost to follow-up in the intervention and control groups. It was also not clear if participants and those assessing outcomes were blinded in this study and if groups were comparable at baseline.

The results are also consistent with studies of booklet-based educational interventions in cancer population conducted in Turkey (Yildirim et al., 2009) and Taiwan (Lai et al., 2004) and pyscho-educational intervention study conducted in northern California (Miaskowski et al., 2004). Participants randomised to the control group received usual care in both the Turkish and Taiwanese studies (Yildirim et al., 2009, Lai et al., 2004), however in the American study they received a general cancer pain guideline booklet (Miaskowski et al., 2004). All studies concluded that participants randomised to the pain education group showed a significant decrease in pain severity

compared to the control group (Yildirim et al., 2009, Lai et al., 2004, Miaskowski et al., 2004).

However both Turkish and Taiwanese studies were single-site and sample sizes were small (Yildirim et al., 2009) and (Lai et al., 2004). These results therefore need to be interpreted with caution because the smaller the study the higher the risk of type I error. Although the sample size was larger (n=174) in the American study and only a small number was lost to follow-up, the majority of the participants in this study were white and well educated. It is difficult therefore to conclude if this evidence transfers to other ethnic groups and less educated populations.

The results are also consistent with video-based pain education interventions conducted among elderly cancer patients in Florida/USA (Clotfelter, 1999) and in Australia (Lovell et al., 2010). Participants received a booklet and watched a video that presented information contained in the booklet about cancer pain management. Both studies concluded that participants who received the video-based pain management intervention reported significant reduction in pain severity compared to participants who received standard care (Clotfelter, 1999, Lovell et al., 2010). However follow-up assessments were conducted two weeks after randomisation in both studies. Although Lovell et al (2010) repeated assessments after four weeks and findings still remained statistically significant it is difficult to infer that outcomes will still remain significant beyond this time period. In the American study sample size was small (n=36). Despite Lovell et al (2010) having a larger sample size (n=217), attrition was very high (35% of the participants were lost to follow-up after four weeks).

While video-based educational interventions may be appropriate for elderly people these may not be feasible and applicable in a Malawian context because the majority of the population have extremely limited resources and live in rural areas where there is no electricity. In Malawi interventions should not be reliant on resources that require equipment and technology that may be only infrequently accessible to the population.

The results are contrary to a comparison of a self-care symptom management education intervention (Gifford et al., 1998) and a symptom management manual (Wantland et al., 2008) in a trial of women with HIV in the USA (Webel, 2010). The study concluded that there were no significant differences between the two groups. It is possible that the author did not find significant results because the study compared two interventions that have already been proven to reduce symptom severity and frequency and moreover the study did not take into account specific factors influencing gynaecological symptoms such as the menopause and childbearing / rearing (Webel, 2010).

The results of the current study are also contrary to a trial of video-based and booklet intervention (Anderson et al., 2004) and a trial of face-to-face discussion approach on steps to cancer pain management (Ward et al., 2008) both conducted in the USA. Both studies concluded that there were no statistical differences on pain severity between the pain management intervention group and the comparison groups (Anderson et al., 2004, Ward et al., 2008). The video-based intervention was also proven not to be effective when tested again but inclusive of family carers as well as patients (Ward et al., 2009). Attrition was low in the former study (14%) (Ward et al., 2008) but

higher in the latter study (32%) (Ward et al., 2009). Perhaps both studies did not observe any effect of the intervention tested between the groups because the control group was given a similar level of attention to the intervention group. Moreover clinical recruitment centres where participants were recruited had been involved in pain quality improvement efforts.

8.5.2 Effects of the pain education intervention on patient pain interference

In the current trial participants randomised to the pain education intervention reported greater reduction in pain interference with daily activities compared to those randomised to usual care. The results are consistent with two small trials conducted among cancer patients in Holland (Oldenmenger et al., 2011) and patient/carer dyads conducted in Taiwan (Lin et al., 2006). Pain interference in the Dutch study was evaluated using multiple teaching methods including an information brochure, consultations with pain consultants and palliative care nurses (Oldenmenger et al., 2011). In the Taiwanese study intervention participants received a pain education booklet, an ongoing reiteration and face-to-face discussion. Those who received the intervention experienced a significant reduction in pain interference compared to patients who received standard care. Perhaps both studies produced significant results because in the Taiwanese randomisation was at dyads level (patient/family). This is in line with the present study because patient and family concerns are often correlated (Lin, 2000). In the Dutch study the

results were significant possibly because of using a number of teaching methods. More participants were lost to follow-up in the intervention group (26%) compared to those lost to follow-up in the control group (11%) in the Dutch study. In contrast to the present study, a trial conducted amongst women with gynecological cancer in the USA (Ward et al., 2000) and another among hospitalised cancer patients in Taiwan (Lai et al., 2004) observed no differences in the effect of an information booklet and five consecutive days of face-to-face discussions with a nurse respectively. The control group received usual care in both studies, but in the study by Lai et al (2004) the control group was visited by a research nurse for five days, but did not discuss anything about the intervention. This may partly explain the lack of observed effect. Both trials had small sample sizes. Moreover Lai et al (2004) conducted their study among hospitalised patients so direct comparison with the present study in terms of pain interference with activities is difficult. Moreover in both studies there was lack of detail provided as to what constitutes usual care.

Video-based pain educational interventions have been reported to be ineffective in reducing pain interference in trials among cancer patients in Australia (Lovell et al., 2010) and the USA (Anderson et al., 2004). In both studies around a third were lost to follow-up. Anderson et al (2004) conducted follow-up assessments up to 10 weeks which meant it was possible to observe both short-term and longer term effects of the intervention. Again, a lack of an observed effect may be due to the use of video in both groups. For the non-interventional group the content of the video was restricted to nutritional

management, but the attention paid to watch the video might in itself reduce pain interference (Anderson et al., 2004) .

A systematic review (Bennett et al., 2009) retained twenty one trials (ninteen where treatment was randomised) and concluded that pain educational interventions are not effective on improving pain interference among cancer patients. However this review excluded pain interference outcomes before and after four weeks follow-up. Over two-thirds of the trials included in this review had methodological limitations such as lack of details about concealment allocation.

8.5.3 Effects of the pain education intervention on patient pain knowledge

Participants in the pain education intervention reported a greater improvement in knowledge on pain management compared to participants in the usual care group. The results of the current study are consistent with trials examining the effects of pain education interventions on knowledge conducted in France (Goujard et al., 2003), Taiwan (Chiou et al., 2004) and South Africa (Peltzer et al., 2012) delivered through group (Peltzer et al., 2012, Goujard et al., 2003) or individual sessions (Chiou et al., 2004). Participants who attended educational sessions on management of HAART side effects and adherence counselling showed a significant improvement compared to participants who received usual care (Peltzer et al., 2012, Chiou et al., 2004, Goujard et al., 2003). Even though there was no attrition in the Taiwanese study, sample size

(n=67) was small (Chiou et al., 2004). Attrition was low in the South African study (4%) and the sample size appeared adequate (n=152). Blinding of the assessor was not described in either study. Contamination was reported in the French study, 19 of 179 participants in the usual care group attended education sessions, however it is not clear if intention-to-treat analysis was conducted (Goujard et al., 2003).

The results from the current study are consistent with educational intervention studies consisting of an information leaflet conducted in South Africa (Dowse et al., 2014) and India (Rajesh et al., 2013) on the management of pain due to side effects of HAART. However in the study conducted in India an information leaflet was augmented by adherence counselling by the pharmacists (Rajesh et al., 2013). The authors reported that participants who received the intervention showed a significant improvement in knowledge about side effects of HIV treatment compared to participants randomised to the control group (Dowse et al., 2014; Rajesh et al., 2013). Self-efficacy improved significantly in the intervention group (Dowse et al., 2014), adherence and attitudes towards HAART improved significantly in the intervention group (Rajesh et al., 2013). In the South African study attrition was high, 50% of the participants were lost in the intervention group and 39% were lost in the control group although it is not clear why there was such high attrition. Furthermore the authors did not describe how outcomes were measured and whether or not the person conducting these was blind to treatment allocation. This was a problem shared by Rajesh et al which also

failed to report details of randomisation or any attempts to conceal treatment allocation.

The finding of improved patient pain knowledge from the current study are also consistent with the positive results from two trials of pain management education programmes conducted for cancer patients conducted in the Netherlands (de Wit et al., 1997) and Australia (Yates et al., 2004). The Dutch study used a multi-method approach consisting of verbal instructions, written materials, audio cassette tape, and pain diaries. In the Australian study participants attended education sessions on communicating pain problems, personalized pain management plan and addressing barriers to pain management including a booklet. In both studies the process of randomisation is poorly described. Follow-up assessments were conducted after one week in the Australian study. It is not possible to conclude if the positive benefits observed will be sustained beyond this very short time period.

Similarly, a pain educational intervention consisting of a pain hot line toll-free number to call or a weekly telephone call group consisting of four telephone calls from an oncology nurse specialist over a month has been shown to be effective in improving knowledge and beliefs about cancer pain compared with standard care (Wells et al., 2003). This study is similar to the current study because it recruited both patients and carers as study participants. However participants were predominantly white (92%). The sample size was small and half of the participants did not complete follow-up assessments after six months.

The results of the current study are contrary to a randomised controlled trial among men with symptoms of HIV/AIDS who were taught skills on self-management of pain such as relaxation and physical exercise. The control group received standard care. The study concluded that knowledge levels improved in the control group compared to the experiment group (Gifford et al., 1998). Recruitment was restricted to male participants, besides this was a pilot study as such it is not appropriate to make conclusions about effectiveness.

8.5.4 Effects of the pain education intervention on patient quality of life

Participants in the pain education group experienced a better quality of life than participants in the usual care group. In the current study quality of life was evaluated using the APCA African POS. One aspect of quality of life in the APCA African POS is spirituality. Meeting patients' spiritual needs is a step towards providing holistic care in the pain management of the HIV/AIDS population. The WHO recommends holistic management of pain (WHO, 1998). This is important because research has shown that people who have been diagnosed with HIV/AIDS are more likely to be depressed because they are uncertain about their future (Sherr et al., 2011). A mixed-methods study (Selman et al., 2013) conducted in South Africa and Uganda among patients with chronic conditions such HIV/AIDS and cancer reported that there is evidence that meeting patients' spiritual needs can improve their quality of life

and satisfaction with care. Perhaps in the current study the improved quality of life observed among people in the pain education group was partly explained by feeling more cared for by a health care worker who spent time with them and, where possible, followed this up with a telephone call. It is difficult to know exactly how spiritual well-being played a role here due to the absence of qualitative data. Within the APCA African POS spirituality is understood as 'peace and life worthness' for people with incurable diseases in sub-Saharan Africa (Selman et al., 2013). Participants of the Selman study interpreted peace and life worthness as a perception of their own self and their place in the world, relationships with others, spiritual beliefs, health and health care. Patients may prioritise spiritual wellbeing over physical dimensions of quality of life (Selman et al., 2012).

The results from the current study are consistent with other studies among HIV/AIDS patients (Chiou et al., 2006a, Lechner et al., 2003, Inouye et al., 2000). In a study conducted in Taiwan (Chiou et al., 2006a) and the USA (Inouye et al., 2000) quality of life was evaluated using the Quality of life Index (Ferrans and Powers, 1985) which measures level of satisfaction with different aspects of life. The Taiwanese study consisted of a symptom management programme delivered either as one-on-one or in a group intervention (Chiou et al., 2006a). The American study consisted of a self-management training for symptoms of HIV/AIDS (Inouye et al., 2000). Both intervention groups showed a significant improvement in quality of life compared to the control group (Chiou et al., 2006a, Inouye et al., 2000). Sample size was small in the Taiwanese study, and participants were not

assigned to groups at random. Therefore allocation bias cannot be excluded. Recruitment of participants from one city in Taiwan limits what can be generalised from the findings. However all participants were successfully followed-up (Chiou et al., 2006a). In the American study, the sample size was also small and the level of attrition was unclear (Inouye et al., 2000).

In another study (Lechner et al., 2003) quality of life was evaluated using the Medical Outcomes Study Health Status Questionnaire for HIV. Participants were randomised to receive either group-based cognitive-behavioural stress management/expressive-supportive therapy or individual psycho-educational intervention. The study concluded that group-based intervention was more effective in improving quality of life than individual psycho-educational intervention. Both interventions were effective in improving cognitive function, health distress, mental health and health perceptions (Lechner et al., 2003). However despite being a large study (n=330), participation was restricted to female participants who were predominantly poor with low socio-economic status, this limits generalisation to other women with a stable income, The study design involved two intervention groups without a standard control group.

Findings from the current study are consistent with individualised telephone-based educational interventions (Wang et al., 2010, Catz and Balderson, 2014) conducted in China (Wang et al., 2010) and in the USA among older patients (Catz and Balderson, 2014) to promote adherence and improve quality of life. The studies concluded that a medication adherence intervention improves quality of life (Wang et al., 2010, Catz and Balderson, 2014). In the

Chinese study participants who received the intervention were more likely to be adherent compared to those who did not receive the intervention (Wang et al., 2010). Family carers were also invited and participated in the discussion during home visits although they were not participants in the study. However adherence was measured through self-report without any objective measure such as pill count. These results need to be interpreted with caution due to risk of social desirability bias. The American study had a larger sample size (n=452) and diverse ethnic group participants, and the authors used a strict intention-to-treat strategy (Catz and Balderson, 2014) however it is not clear how many participants were lost to follow-up.

The results are consistent with a large randomised controlled trial (n=1140) of a group-based self-management education programme among patients with chronic conditions such as cancer, asthma, stroke, heart disease and lung disease (Lorig et al., 1999). Participants who were randomised to the control group attended the programme after completing follow-up assessments at six months. The study concluded that participants who received the intervention showed a significant improvement in health behaviour and health status (Lorig et al., 1999). Attrition rate was low in this study (18% were lost to follow-up). Even though the study had a heterogeneous sample of participants with different chronic conditions, none of the study participants had HIV/AIDS. It is difficult to conclude if the positive benefits observed is applicable to patients with HIV/AIDS.

Findings from the current study are in sharp contrast to other studies in the same HIV/AIDS field (Goujard et al., 2003, Webel, 2010) on the effects of pain

education on quality of life. In a study conducted in France participants randomised to the intervention group attended individualised education sessions while those randomised to the control group received standard care, but were invited to attend sessions upon completion of follow-up assessments (Goujard et al., 2003). In another study conducted in the USA, HIV positive women attended a peer-led group session while the control group received a copy of the HIV symptom management manual (Webel, 2010). It was concluded that there were no significant differences between the two groups on quality of life over three months (Webel, 2010) and over six, 12 and 18 months (Goujard et al., 2003). This may have been due to a ceiling effect in the French study with participants at baseline reporting good quality of life (Goujard et al., 2003). Apart from the small sample size (n=89) in the American study, the population was restricted to women and the intervention did not target the specific pain related gynaecological problems that women experience such as menopause. The other explanation as to why the study did not observe any difference may be due to participants in the control group receiving a pain management manual previously found to be effective in reducing the severity and frequency of physical, psychological and gynaecological HIV/AIDS related symptoms (Wantland et al., 2008).

8.5.5 Effects of the pain education intervention on carers knowledge

Family carers randomly allocated to the pain education intervention group showed a greater improvement in knowledge compared to family carers randomly allocated to the control group.

This is consistent with a psychosocial interventional study conducted in Australia among family carers and patients with HIV/AIDS (Pakenham et al., 2002). The intervention consisted of counselling sessions delivered to either family carers with their patients or family carers alone. The control group received standard care. The study concluded that family carers who attended sessions with their patients showed significant improvement in knowledge compared to family carers who attended alone or who did not. Likewise patients who attended sessions with their carers showed significant improvement in knowledge compared patients who did not. These findings suggest that intervening at carer giver/carer recipient level produces better outcomes than intervening at individual carer giver level (Pakenham et al., 2002). There were a number of methodological concerns in the Australian study. The sample size was small, thus limiting statistical power and generalizability to the wider population. Some participants were not randomised, but were assigned to the treatment group because of their condition, this has potential for allocation and performance bias.

Similarly a three-month group-based education session to improve knowledge and skills on care provision conducted among 202 elderly family carers in South Africa, concluded that participants who attended all the sessions showed

improved knowledge and skills in HIV/AIDS management, were more positive towards people living with HIV/AIDS, and more willing to provide care to their dependants, than participants who attended part of the sessions or none of the sessions (Boon et al., 2009b). This study did not have a control group and 13 participants attended part of the sessions and 48 did not attend any sessions at all. It is difficult to infer if the positive benefits observed would still be observed if there was a randomised comparison with a control group.

Similarly a systematic review of interventions for carers in the UK reported that educational programmes consisting of written information, interactive group sessions and individual sessions for carers of people with dementia are effective in improving knowledge levels (Victor, 2009). Although in this review only one study was a randomised controlled study and two other studies were non-RCT and qualitative designs. Non-RCT and qualitative study designs do not provide stronger evidence compared to an RCT because of the risk of bias.

8.5.6 Effects of the pain education intervention on carers quality of life

Carers in the pain education group reported a better quality of life than carers in the usual care group. The results are consistent with other studies among carers of people living with HIV/AIDS (Rotheram-Borus et al., 2001, Pakenham et al., 2002, Pomeroy et al., 1995, Smith Fawzi et al., 2012) although different tools were used in each study to evaluate quality of life.

In one study (Rotheram-Borus et al., 2001) conducted in New York parents of adolescent children were randomly allocated to attend group-based education sessions on topics such as coping with HIV/AIDS illness, coping with fear and anger, child caring, creating a positive home, while the control group received standard care. The study concluded that participants randomised to the intervention group reported a reduction in quality of life in the domain of anxiety, depression and distress compared to participants in the control group (Rotheram-Borus et al., 2001). However it is not clear who conducted outcome assessments and if they were blind or not, so the possibility of detection bias cannot be excluded.

In another study a psychosocial intervention was delivered to family carers of HIV/AIDS patients either with their patients or family carers alone in Australia (Pakenham et al., 2002). Family carers who received the intervention with those they cared for showed a significant improvement in quality of life in the domain of global distress, dyadic adjustment. Likewise patients who received the intervention with their family carers showed an improvement in quality of life in the domain of dyadic adjustment, social adjustment, target problems and subjective health status (Pakenham et al., 2002).

In a quasi-experimental study a psychosocial support intervention was delivered among families affected by HIV/AIDS in Haiti (Smith Fawzi et al., 2012). Caregivers (n=130) most of whom were HIV positive themselves (95%) attended a psychosocial intervention on coping with challenges of HIV infection, problem solving skills, care provision to children, and reducing emotional distress. The study concluded that caregivers demonstrated a

significant reduction in depressive symptoms and improved social support (Smith Fawzi et al., 2012). Importantly the study did not have a control group to provide a definitive estimate of effect of the intervention.

However in this study participants were not randomised, but self-selected to receive the intervention or usual care. This has potential for selection bias. Unsurprisingly groups were not equivalent at baseline with systematic differences between the two groups other than in terms of the intervention received making it impossible to know the reasons for any change in outcome. A psycho-educational group-based interventional study among family members of people with HIV/AIDS recruited 33 family members who attended eight sessions covering positive living, physical aspects of HIV illness, and carer empowerment in care giving, coping skills, and dealing with challenging life events. The study reported positive outcomes in the intervention group compared to participants in the control group in terms of stress, stigma, depression, and anxiety, but there were no significant differences between the intervention and control groups in terms of social support (Pomeroy et al., 1995). This may be due to outcomes being measured immediately after the delivery of the intervention, which may not be sufficient for participants to feel that other group members were part of the support system. The other explanation may be due to the fact that levels of depression were very high among study participants, research has shown that depressed people have lower levels of perceived social support (Sherr et al., 2011, Eller et al., 2013). However in this study participants were not randomised, but self-selected to receive the intervention or usual care. This has potential for selection bias.

Because of this groups were not equivalent at baseline with lack of randomisation to have generated systematic differences between the two groups other than in terms of the intervention received.

A meta-analysis of psycho-educational, skills training and therapeutic counselling interventions for family caregivers of cancer patients examined 19 randomised controlled trials and concluded that such interventions had small to medium effects on reducing caregiver burden, improving caregiver ability to cope, increasing their self-efficacy and improving some aspects of quality of life (Northouse et al., 2010). However the majority of participants in the studies reviewed were Caucasians (84%), this limits generalizability to other races and ethinic groups.

The results of the current study are contrary to studies conducted in the USA on the effects of education intervention on carers quality of life, focussing on a boosting social support intervention among parents of children with HIV/AIDS (Hansell et al., 1999) and a psycho-educational study among partners of patients with HIV/AIDS (Gordon-Garofalo and Rubin, 2004). Attrition was higher in the former study and all participants who were lost to follow-up were excluded from the analysis, this raises questions on attrition bias.

In the latter study participants were not randomised, but assigned to groups basing on their preference resulting in group imbalance and self-selection bias. There were (n=19) participants in the intervention group and (n=9) participants in the wait list control group (Gordon-Garofalo and Rubin, 2004).

8.5.7 Positive aspects of care giving/motivation and other related outcomes

Carers in the pain education group reported greater motivation to provide care than carers in the usual care group.

The results of the current study are consistent with group-based psycho-educational intervention studies conducted in Australia among family carers of patients with advanced cancer (Hudson et al., 2008, Hudson et al., 2009). Both studies focussed on caregiving preparation, self-care strategies, symptom management strategies and rewards in caregiving. It was reported that family carers showed adequate preparation, and were more competent, prepared and motivated to provide care after receiving the intervention. However neither study included a control comparison group. It is therefore impossible to adjust for regression to the mean or social desirability bias making it hard to estimate the effect of the intervention.

Similarly a multi-method psycho-educational intervention study consisting of home visits, face-to-face discussion, phone call, booklet and audiotape, focussing on carer giver motivation, self-care strategies, and caregiver preparation reported that family carers who received the intervention showed a significant improvement in motivation to provide care compared to family carers who did not. However there were no differences observed on preparation to provide care, competence and anxiety (Hudson et al., 2005a). Perhaps lack of significant improvements on anxiety and other outcomes was because the intervention included both current carers and bereaved carers.

Presumably bereaved carers were anxious having lost their loved one. Furthermore, the distribution of caregivers' scores were skewed suggesting that they typically circled either very high or very low scores on a scale. This raises the issue that differences may be obscured by looking at mean differences as a result of ceiling and floor effects.

Similarly a quasi-experimental study conducted in Sweden among family carers of patients with life-threatening conditions reported that a group-based supportive and educational programme showed a significant improvement in caregiving preparation, competence in caregiving and rewards for caregiving compared to standard care (Henriksson et al., 2013). However this was not a randomised controlled trial and the two groups were non-equivalent. Although both groups were similar at baseline it is not possible to exclude unknown confounding and allocation bias.

A qualitative study of 47 primary family caregivers of cancer patients conducted in Australia concluded that even though family carers experience challenges such as lack of skills to manage symptoms, lack of support from health care workers and challenges with their own health, 60% of the caregivers reported positive aspects such as having an improved relationship with the person they care for, becoming stronger and more confident with care provision and improved communication. However, some participants reported disliking the act of caring in spite of having a close relationship with the person who needed care (Hudson, 2004). -

Similarly in a study among family caregivers of patients on palliative care conducted in Canada, participants were asked to identify and report any positive aspect of their role. Of the 289 family caregivers, 211 (70%) reported at least one positive aspect and 20 caregivers (6.9%) reported more than one positive aspect. Caregivers who reported more than one positive aspect were less likely to report depression, burden or poor health (Cohen et al., 2002).

8.5.8 Effect of the intervention on patients use of medication

Participants who were randomised to the pain education intervention were six times more likely to be prescribed Codeine and five times more likely to receive Diclofenac compared to participants randomised to the usual care group. In Malawi, Codeine and Diclofenac are usually prescribed and administered to patients who do not respond to WHO step one pain medication such as Panadol, Brufen and Aspirin. Participants in the pain education group were taught how to assess pain and how to classify pain. They were also taught how to manage pain and examples of drugs were listed based on the severity of pain (See Appendix 13 Information leaflet). Since participants showed improvement in knowledge after receiving the intervention it is possible that they used this information to express themselves freely to the doctor or nurse about their pain and how they responded to treatment. This possibly influenced the doctor in the way they prescribed.

The results of the current study are in contrast with a randomised controlled trial among cancer patients conducted in California. In this study patients in

the intervention group received a self-management pain education programme facilitated by a specialist trained oncology nurses. They were taught how to use a pill box, were given written instructions on how to communicate to physicians about unrelieved pain and changes to analgesia prescriptions. The control group received a cancer pain management guideline booklet. The study concluded that there were no significant differences between groups on opioid analgesic prescriptions and intake, even though on average the intervention group had an increased change of analgesia prescribed compared to the control group (Miaskowski et al., 2004). The booklet which the control group received might have helped the participants to respond positively like the intervention group.

The results of the current study showed that there were no significant differences between the pain education group and the usual care group on Brufen and Panadol received at follow-up. Perhaps this is due to the fact that in Malawi, it is very common for patients to be prescribed Panadol and Brufen. These are also the drugs the patients can easily obtain over the counter.

8.5.9 Association of baseline factors with outcomes

In the current study, younger participants experienced a greater reduction in pain severity compared to older participants. This may be due to the fact that with old age people experience other health related problems such as chronic arthritis, musculoskeletal pain (Walker et al., 2012) and back pain (Hider et al., 2011). Even though arthritis can occur at any age (Walker et al., 2012)

people with old age are more likely to have the condition because their immune system becomes weaker with age and therefore they become more susceptible to inflammatory arthritis. An epidemiological study reported that the prevalence of back pain is associated with age (Andersson, 1999), however another study (Breitbart et al., 1996) reported no association between age and pain severity.

The results of this trial show that pain interference was associated with age and gender of the participants. Participants who were older experienced worst pain interference compared to participants who were younger. Females experienced worst pain interference compared to males. This may be due to the fact that as people become older they are less able to tolerate exercise and are less likely to follow an exercise regime if they have painful conditions such as back pain and arthritis (Walker et al., 2012), as these are closely associated with age (Andersson, 1999). Women experienced worse pain interference than men possibly due to the fact that traditionally women are more likely to be caregivers. Unlike men, women are more likely to have to look after themselves even when they are feeling unwell in the presence of a man. Another possible explanation could be due to the fact that the intervention did not provide specific information about gynaecological pain symptoms which women experience. One trial (Webel, 2010) reported no differences on symptom status among women with HIV, but the same intervention reported differences in symptom status among men with HIV/AIDS (Gifford et al., 1998). Qualitative interviews with women after the intervention reported that the intervention did not contain specific information

about gynaecological problems (Webel, 2010). Similarly a study of pain syndromes among ambulatory AIDS patients found women more likely to be diagnosed with headache than men (Hewitt et al., 1997). A review of literature on gender variations and clinical pain experience concluded that women are more likely to experience recurrent pain than men. They are more likely to experience severe headache, abdominal and facial pain than men (Unruh, 1996). A study to examine the relationship between gender and pain reported that women report higher pain ratings, poorly tolerate pain and show more concern about how pain affects their daily life (Vallerand and Polomano, 2000). The experience of pain differs between men and women often due to biological, physiological (Zubieta et al., 2002) and psychological (Campbell et al., 2003) differences. Men and women may also respond differently to both pharmacological and non-pharmacological pain management interventions (APCA, 2012).

The results of the current study showed that quality of life of the patient (palliative care outcomes) was associated with age and gender. The mean score for females was four points lower (worse) compared to males. Perhaps this may be due to the fact that females experienced greater pain interference compared to males. In African settings, females are more likely to be under-treated for pain than males and are likely to be more anxious than males which exacerbates poor quality of life (APCA, 2012). Moreover the gynecological pain syndrome as a result of HIV infection also contributes to poor quality of life (Webel, 2010).

8.6 Implication for training in pain education

The pain education intervention consisting of an information leaflet, face-to-face discussion and follow-up phone call reminder was simple to design and administer. It offered substantial benefits to the HIV/AIDS patients and their family carers. It was relatively cheap and simple to design. Nurses put much emphasis on medication adherence but sometimes overlook the issue of side effects of HIV/AIDS medication and how to manage them particularly when they are faced with heavy workloads and limited time. However if patients have limited information about managing their pain they are likely to return to the hospital to seek advice on how to manage the condition. Nurses tend to focus their attention on the pharmacological management of pain. This is partly due to the lack of a thorough method of assessment of pain for HIV/AIDS patients.

Comprehensive pain assessment is important because it will help doctors, nurses to come up with a proper treatment plan that embraces both pharmacological and non-pharmacological management strategies. Pain assessment will enable doctors and nurses to rate patient's pain and classify it accordingly. This may enable them to select appropriate drugs and other interventions for the patients.

Even though this study did not evaluate the effects of pain assessment, the results support the importance of incorporating it into clinical practice so that every patient should have a record of pain assessment to provide a guideline

for pain management. The evidence produced by this study lends strong support to this approach.

While this study does not provide evidence for the importance of pain education among student nurses, in order to improve the practice and care for HIV/AIDS in the clinical setting, there is a need to incorporate pain assessment and pain management in the training of nurses in Malawi. After nurses have qualified they will have knowledge and skills on pain management among HIV/AIDS patients. This will enable them to use these skills in clinical practice.

A study conducted in east Africa among nurses who received end of life education and training reported that participants rated the curriculum as being excellent and they appreciated the knowledge and skills they acquired through the three day course (Paice et al., 2010). Similarly a postgraduate course on palliative care among medical doctors in South Africa led to participants acquiring clinical palliative care skills with a recommendation that the training should be introduced to undergraduates (Ens et al., 2011). The training of nurses on the management of pain is an important recommendation if the evidence from this study is to be incorporated into routine practice. In Malawi, nurses and clinical officers who prescribe and administer HIV medication do receive training for them to carry out this role; however the training package does not include the holistic management of pain in HIV/AIDS (Ministry of Health, 2011a, Ministry of Health, 2014).

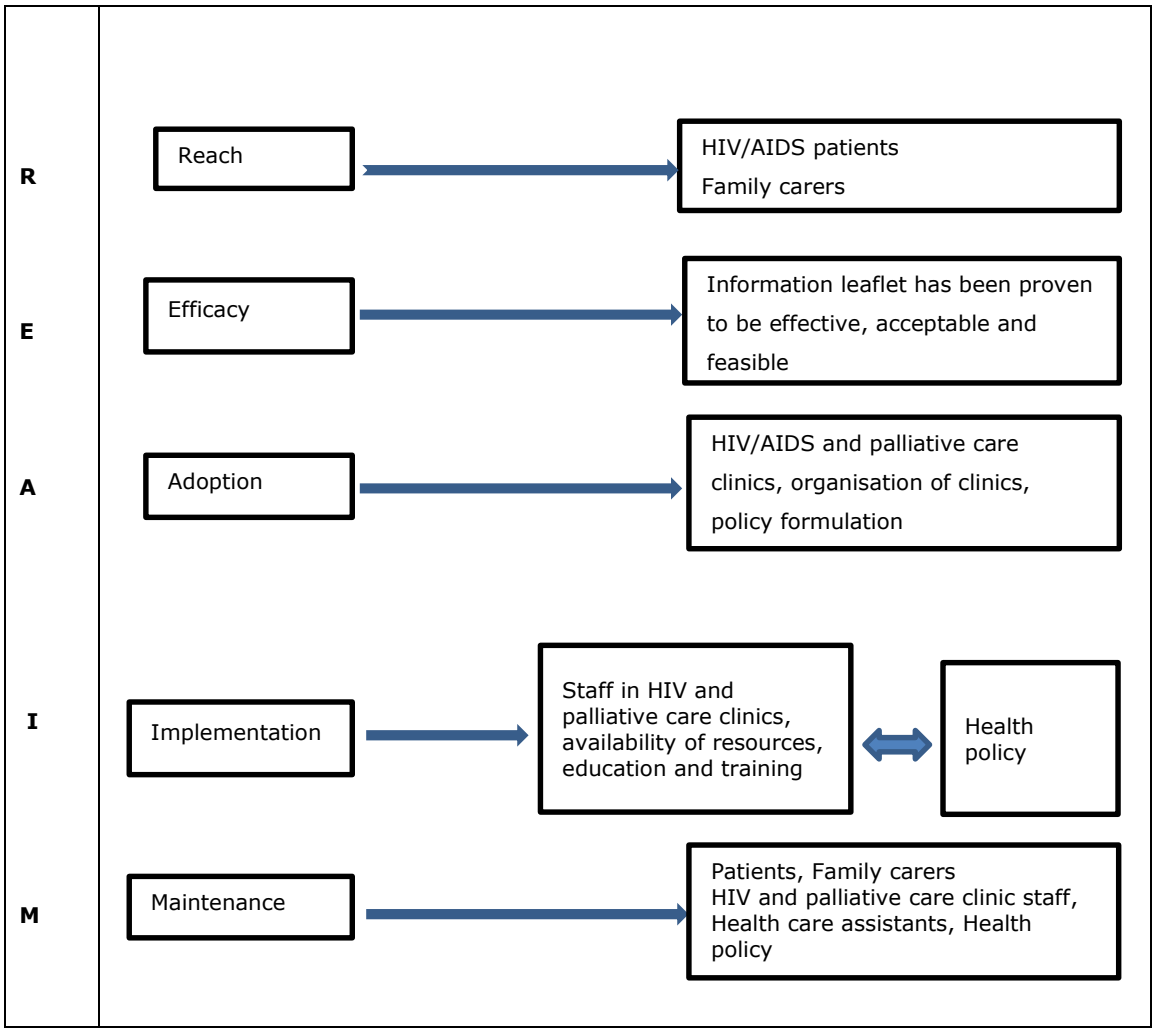
The government in conjunction with the Palliative Care Association of Malawi have invested in the training of nurses as palliative care co-ordinators. The training package on palliative care includes topics such as symptom assessment and management, pain assessment and pain management using both pharmacological and non-pharmacological interventions. However despite these initiatives, many districts are not effectively providing palliative care services due to funding. Furthermore of those few nurses and clinical officers who have been trained in palliative care; many do not implement this into the routine care of their patients perhaps due to time pressure and workloads. However stronger evidence suggest that if busy practices can redesign their care, they can provide better care than standard care (Renders et al., 2001).

Funding for health services in Malawi comes from the central government, but as part of decentralised management, each district plans their own services. The senior management teams in some districts do not prioritise palliative care services. Therefore even though nurses may receive training, implementation of their knowledge and skills is vital and calls for additional resources and focus (Malawi Government, 2012b).

The RE-AIM (Reach Efficacy Adoption, Implementation and Maintenance) framework (Bonomi et al., 2002) could be adopted to implement the pain education intervention that was found to be so effective in the present study. RE-AIM is an implementation science model that directs attention to issues or challenges faced to disseminate and implement evidence-based programmes or policies in the management of chronic illnesses such as HIV/AIDS (ElZarrad et al., 2013). Adopting this pain education intervention will require

disseminating study findings to the institutions where the study was conducted and to HIV/AIDS patients and plan the modalities of implementing the intervention into routine care. The nurse-led pain education intervention study has been shown to be effective in the management of HIV/AIDS pain in two public hospitals in Malawi. Figure 17 below summarises the proposed adoption of the RE-AIM model in the management of pain in HIV/AIDS palliative care clinics in Malawi. The RE-AIM implementation science model considers both individual (Reach and Efficacy) and system (Adoption and Implementation) levels and it emphasises both the importance of external (Reach and Adoption) and internal (Efficacy and Implementation) validity (Glasgow et al., 2001).

Figure 18: Adoption of the RE-AIM model in the management of pain in HIV/AIDS and palliative care clinics in Malawi



From informal observation at both the HIV/AIDS clinics in Ekwendeni and Mzuzu central, it was apparent that while some staff members saw health education as part of their role, others did not. Perhaps this is the problem of

attitude of some health care workers. One way to deal with this is by asking HIV/AIDS Coordinators to develop a monthly or weekly rota for health education provision on pain management among HIV/AIDS patients. The clinic co-ordinators should ensure that staff members are implementing health education, for instance at Ekwendeni hospital the rota was there but there was no implementation among staff members. Implementing the pain education intervention will require a participatory approach perhaps guided by the theory of change (De Silva et al., 2014) and the normalisation model of implementing complex interventions (May, 2006). Both approaches suggest bringing together different stakeholders such as HIV/AIDS patients, family members, and healthcare workers including hospital managers and decision makers to discuss the best approach and sustainable way of implementing the intervention. The Medical Research Council framework for complex interventions suggests that for implementation to take place, evidence from the study needs to be presented to decision makers and other stakeholders in a persuasive manner (Craig et al., 2008).

Through my observation at Mzuzu central hospital, health care assistants were involved in provision of health education to patients newly registered to start treatment. I attended some of the sessions and observed that they were conducted and delivered in a similar manner as those delivered by qualified staff nurses and clinical officers. I would therefore recommend that the institution should actively involve health care assistants to provide health education on pain management to the patients in situations where workload is high and time is under pressure. Health care assistants would need basic

training on pain assessment and management. This will enable patients and their family members to acquire skills and knowledge on pain management at home. The same model of using health care assistants is utilised in Malawi in the provision of counselling and testing services for patients with signs and symptoms of HIV/AIDS. The model has helped HIV/AIDS patients to start treatment within weeks after diagnosis rather than waiting for three months (WHO, 2011b).

Student nurses need to receive education on pain assessment and management. Palliative care training might be effectively delivered using the existing nursing and clinical training to reduce overload from new skills and frameworks of care (Harding and Higginson, 2005). Palliative care needs to be incorporated in the nursing curriculum, so that as nurses graduate they have basic skills and knowledge in pain assessment and management. For instance student nurses conduct a case study on providing health education and care to a client seeking family planning services, the same model could be extended to the management of pain in HIV/AIDS.

While this study does not provide evidence for the importance of pain education among student nurses, in order to improve the practice and care for HIV/AIDS in the clinical setting, there is a need to incorporate pain assessment and pain management in the training of nurses in Malawi. After nurses have qualified they have knowledge and skills on pain management among HIV/AIDS patients. This will enable them to use these skills in clinical practice.

Healthcare workers and staff from Non-Governmental organisations provide symptom management and basic nursing care to patients and their families. However there is no consistency and continuity in implementing such activities. It depends on availability of funding. It is therefore recommended that health care workers should teach families and patients during home visits pain assessment and pain management skills so that patients and families can be prepared and be equipped to carry out this role at home. Volunteers and other informal carers who are involved in providing home health care need basic training on pain assessment and pain management. The training of volunteers at present mainly focusses on basic nursing care; moreover some volunteers have not been trained. It is recommended that the untrained volunteers should also be trained. This may help them to utilise the skills and knowledge gained in providing holistic care to patients who are in pain in their role as informal caregivers. However this will require resources if training is to be conducted. Furthermore some informal carers easily quit if they experience carer burden and burn out (Malawi Government, 2011).

HIV/AIDS staff members need basic training on health education among patients and carers on pain management. My experience of working in the medical wards as a student nurse and as a qualified member of staff was that pain assessments were not conducted with both in patients and out-patients. There was nothing like recording the pain scores for monitoring progress. This is possibly because staff nurses do not have basic knowledge about pain assessment and pain management and use this knowledge to provide care to the patients. It should be emphasised to all nurses that assessment of pain

should be conducted and recorded in the same manner vital signs such as blood pressure, temperature, respirations and heart rate are conducted and recorded. This will enable proper monitoring of the patient's condition, and the management of pain based on the severity of pain (depending on availability of treatments). This will also help the nurse to identify other interventions to manage pain.

Non-governmental organisations that are involved in providing training and home-based care to informal carers should consider supporting hospitals with the implementation of pain management for people living with HIV/AIDS. This may be through provision of funding for the hospitals to design and print information leaflets on pain assessment and management so that patients, family carers and informal carers can use them at home and refer to it as they provide care to their patients. Equally the Malawi government through Ministry of Health and the HIV/AIDS health education unit together with the National HIV/AIDS Commission should consider providing financial support to hospitals to design and producing information leaflets and posters on pain assessment and management which can be distributed to patients who are HIV positive and their families in the HIV clinics and medical wards.

8.7 Implications for policy and pain education practice

8.7.1 Policy formulation

The WHO public health strategy on palliative care was endorsed by organisations in sub-Saharan African (Ddungu, 2011). The policy recommendations from the pain education intervention study are based on the pillars of the WHO public health strategy for palliative care which calls on governments for a national strategy to improve access to palliative care services including the management of pain, health education for health care workers in HIV and palliative care clinics, health education to patients and family members including the community, availability of drugs to treat and manage pain, and implementation mechanisms within the health care clinics (Stjernswärd et al., 2007). Pain education for patients with HIV/AIDS has not received sufficient attention in Malawi hospitals. This is probably due to a lack of formulation of policies and financial support from the Ministry of Health, specifically the Department of HIV/AIDS. There is a need for evidence-based Government policy that will guide the development, design and implementation of HIV/AIDS pain education for patients and family carers. The Ministry of Health through the National HIV/AIDS Director and National Palliative care coordinator need to incorporate pain education among HIV/AIDS patients as part of their HIV/AIDS policy.

The Malawi Government does not have a policy on palliative care. Even though there are national guidelines for palliative care (Ministry of Health, 2009) there is no clear guideline on pain education and management for HIV/AIDS

patients. Additionally the national community home based care policy (Ministry of Health, 2011b) does not explicitly define palliative care and outline activities or services to improve the delivery of palliative care including pain education for people living with HIV/AIDS.

Many have argued that access to palliative care services including relief from pain is a universal human right (Gwyther et al., 2009). The health policy in Malawi must take into consideration the scarcity of resources for pain education and management and the needs of HIV/AIDS patients and their families including community members who are actively involved in providing palliative care services. Policy makers need to make decisions based on evidence for the needs of HIV/AIDS patients and family carers and interventions that are effective in meeting their needs. There is a need for a public health approach in the delivery of pain management to people living with HIV/AIDS and their families. Due to the dearth of research evaluating pain education for HIV/AIDS patients in Malawi and other resource poor countries in the sub-Saharan region, policy making in this area is more likely to be based on international literature and international practice. There is evidence that patient health education in one country may function as a mirror for the quality improvement of the delivery of health education on another country (Visser et al., 2001).

Such policies may trigger health institutions in Malawi to acknowledge the importance of pain education among patients with HIV/AIDS. The policies may trigger the Ministry of Finance through the Department of Treasury to provide financial support for the development of pain education materials such as

leaflets, posters, booklets to be used in practice, training of health care workers, student nurses, patients and family carers, as well as in conducting research in pain education and management. The policy will enable health managers to support nurses in implementing programmes aimed at strengthening palliative care delivery including the management of pain.

8.7.2 Implementation and practice

The findings from this study have great potential to inform the practice of palliative care and HIV/AIDS pain management. Evidence from the study suggests that the management of pain for people living with HIV/AIDS requires a holistic approach focussing on physical, psychological, social, and spiritual aspects of care. In contrast the current practice and delivery of care to patients tends to be limited to the physical aspects of care. This calls for the need to strengthen service infrastructure development so that palliative care and HIV/AIDS management and care is integrated into all forms of care including the management of pain for people living with HIV/AIDS through pain education.

Although the pain education intervention was designed to be simple in this study, it would take approximately 10 to 15 minutes for each patient from a nurses' limited time if it was to be implemented routinely in clinical practice. Even though this intervention was delivered to patients and family carers individually and face-to-face, it can still be implemented and delivered to patients and families through groups, moreover all the patients and families

who attend health education on HIV treatment receive the health education in groups. The pain education intervention may be implemented in a similar manner.

The current practice in hospitals in Malawi including Ekwendeni and Mzuzu central hospital regarding opioids prescription requires only medical doctors and clinical officers to prescribe. Nurses cannot prescribe and they have to refer patients who require an opioid to the doctor or clinical officer. This policy needs to be revised, prescription of opioids need to be extended to nurses just like they are able to prescribe HIV treatment for the patients. Moreover nurses who work in palliative care clinics do prescribe opioids; this can also be extended to nurses who work in HIV clinics and inpatient settings. This model has been found to be effective in other countries in the sub-Saharan Africa such as Uganda where qualified nurses prescribe opioids for pain management (Merriman and Harding, 2010). There is a need to make opioids available and accessible in rural health centres where HIV treatment is offered. This will enable patients who access HIV treatment in rural health centres to also access opioids if they need it. Nurses in rural areas who undergo HIV training also need training to prescribe opioids. Moreover in some rural health centres there are no clinical officers, therefore nurses who work in rural settings should prescribe treatment for the patients, to avoid unnecessary referrals. Similarly in South Africa opioids drugs have been declared essential drugs in primary care settings for the management of cancer pain (Beck and Aocn, 1999). This is in line with WHO foundation measures for HIV pain relief which advocates for the availability of essential drugs, government policy and

education and training. These are essential for palliative care development in African countries (WHO, 2006b, WHO, 1996).

A multi-disciplinary team approach is important to meet the needs of HIV/AIDS patients and their families. HIV/AIDS clinic and palliative care clinic staff need to work with several key players and stakeholders to address the various needs in relation to pain management of HIV/AIDS patients and their families through pain education. There is a complex relationship between physical, social, psychological health of the patients. The intervention tested was developed and delivered using a holistic approach with the guide of the bio-psychosocial model. Pain being physical and biological brings about psychological problems. Pain assessment needs recognising each of these components in order to meet the needs of the patient and family. A study conducted in five countries in sub-Saharan Africa reported that HIV/AIDS patients presented with multidimensional problems (Sepulveda et al., 2003), and this calls for the need for integrated palliative care services.

In the current study Clinical Officers and nurses were involved in the management of patients with HIV/AIDS. Family members and patients were involved in designing and implementing the intervention. Patients were referred for spiritual care if they had a spiritual problem**.** Even though it is not very clear how spirituality played a role in this study, the intervention had a spiritual component. There is a need for a nurse-coordinated multidisciplinary pain management team in HIV/AIDS and palliative care clinics in Malawi. Even though the pain education intervention did not test the effectiveness of a pain management team but this may help in the implementation of pain

management in HIV/AIDS and palliative care clinics in Malawi. The team should be responsible for developing and designing pain information leaflets, train nurses, and other health care workers on pain assessment and management and ensure that health care workers are implementing pain assessment and management skills in their role. The pain management multi-disciplinary team will also be responsible for ensuring that they review patients with pain syndromes and properly develop a management plan of care for the patients. The team should be responsible for monitoring and evaluating pain management education for patients, family carers and health care workers.

Patient involvement is important because they can share experiences on how they have handled a particular situation, for instance which non-pharmacological intervention is better and how exactly they used it. Involvement of family carers is also important because not only do they offer social support, but they complete the family composition. Family support is an important component in the management of pain. The majority of care for patients with HIV/AIDS is provided in their own homes. Home care is cheaper and culturally acceptable for the patient and family members (Jagwe and Barnard, 2002). Additionally in Malawi, family members are involved in caring for the patients in the hospitals due to shortage of health care workers. In Malawi, just like other countries in Africa, we largely rely on family and community support to provide palliative care services (Harding and Higginson, 2005). Personally I have observed nurses frequently conducting bed baths to patients with the support of a family member while working in the hospital. Their presence also strengthens the social support for the patient.

Involvement of the family member in this study helped the patients to remember and reinforce what was discussed during the face-to-face contact. Intervening at patient/family care dyad level is therefore likely to be crucial for this intervention to be effective.

The provision of HIV/AIDS treatment as a therapeutic treatment for people living with HIV/AIDS leaves some patients with palliative care needs unaddressed (Harding et al., 2005, Sacajiu et al., 2009)**.** For instance my personal observation through fieldwork and interaction with staff members working in the HIV clinics suggested that some patients did not take HAART on a regular basis, due to side effects. Pain education is thus important to such patients and their families. A qualitative study among advanced HIV/AIDS patients and their caregivers concluded that side effects of HIV medication and issues surrounding adherence to treatment were the main themes frequently reported by study participants (Sacajiu et al., 2009).

8.8 Implications for research

Findings from the pain education intervention study calls for a number of research activities to be conducted. Findings from this research study need to be disseminated to policy makers, key stakeholders, academicians in order to promote evidence based practice and to examine challenges in implementation. I plan to present the results of the pain education trial at the annual dissemination conference in Malawi to inform practice using the best available evidence. This may enable decision makers to be encouraged to

allocate resources for conducting further studies, and support palliative care activities. This is in agreement with palliative care researchers who argued for a research pillar on the WHO public health strategy (Harding et al., 2013). High quality evidence is needed in order to achieve each pillar of the WHO public health strategy for palliative care (Harding et al., 2013). Furthermore, there is a need to support rigorous and robust palliative care research in Africa in order to inform practice and policies (Harding et al., 2008). In line with this, further research into pain education is a priority, particularly in areas of the world that are resource poor. How this might be successfully implemented is a research question that arises from the present study. A cluster randomised controlled trial could be a vehicle for delivering 'train the trainer' interventions whereby clinics would be randomised to receive such an intervention or not.

In the current study I used tools that have been developed and validated in western countries. Only the APCA African POS has been developed and validated in Africa (Harding et al., 2010b). However for some clients who were not able to understand English, the APCA tool was translated to a local language. However it will be wrong to conclude that the APCA has been validated to the local languages in Malawi, for this reason, I would recommend further research of validation of the APCA African POS into the main local languages used in Malawi. This will enable health care workers in hospitals, HIV/AIDS and palliative care clinics to use the validated tools for monitoring and evaluating palliative care outcomes including pain management programmes for HIV/AIDS patients. Further research is also needed to validate the other tools used in the present study (BPI, Pain Knowledge

Questionnaires, and the Rewards in caregivers in order to evaluate and guide the practice and delivery of palliative care and home-based care programmes.

More research is needed that evaluates pain education interventions and palliative care services applied by health care providers independent from (rather than) research teams. There has been a tendency to underrate the capacity of health care workers to carry out studies of complex interventions and to understand concepts such as randomisation and blinding. However researchers are not frequently involved in clinical practice and implementation of research findings becomes a challenge. There is need to involve health care providers in research activities and this can be a starting point to encourage them to conduct their own studies in future (Mantzoukas, 2008). In addition, the success of many research projects can be attributed to the support from health care workers. The health care workers in the current study were not experienced researchers, but they were highly motivated and maintained enthusiasm for this project throughout the introduction of the study and the last follow-up assessment. Moreover it was for the first time most of them were involved in randomised controlled trial. The successful recruitment of the study participants and low attrition rate is attributed to the staff working in HIV/AIDS and palliative care clinics of the two study settings.

The pain education study was feasible and could be safely incorporated into routine HIV/AIDS pain management in HIV/AIDS and palliative care clinics. Exploring possible ways in which the intervention could be incorporated into routine practice is a priority for future research. In addition more research is needed regarding the components of the pain education intervention. The

current intervention had three main components (1) information leaflet (2) face-to-face discussion and (3) phone call reminder. The design of the intervention did not attempt to find out how the intervention worked, because qualitative interviews were not conducted upon completing follow-up assessments, it is therefore difficult to know which part of the intervention was responsible for the benefits observed.

In the current study, follow-up assessments were conducted eight weeks after randomisation. Future research should consider conducting follow-up assessments at least two or three times and after 12 to 18 weeks to evaluate the pattern of response among participants on long term effects of the intervention.

The views of the participants who took part in this study were not elicited after follow-up assessments. Their experiences about being part of the intervention would have helped to plan and improve the delivery of the intervention. Future research should therefore consider conducting interviews from study participants in order to examine their experiences about the context and process of the intervention and concepts such as randomisation. Such qualitative interviews will also help to answer questions regarding how and why the intervention worked, and how it can be improved.

8.9 Summary of recommendations

On the basis of conducting the trial of pain education among HIV/AIDS patients and their family carers I recommend the following:

- Based on the evidence that pain education intervention reduces pain severity among patients with HIV/AIDS, it is recommended that palliative care clinic staff should provide health education to the patients and their family carers on pain assessment and management. HIV clinic staff should use the same model of providing health education to patients and family carers on drug adherence during registration for new patients and follow-up care for routine appointment patients and family carers.
- Based on the evidence that pain education intervention reduces pain severity, it is further recommended that the Malawi Government should train health care assistants to provide pain education in the clinics. This may help to ease the workloads the nurses and clinical officers' experience. The model of using health care assistants has been reported to hasten HIV testing services in the clinics rather than waiting for nurse counsellors who are overloaded with other nursing services. This is about implementation of the pain education intervention, even though the intervention did not test the effects of using health care assistants.
- The Malawi Government and non-governmental organisations should train family carers on pain and symptom management. This is on the basis that pain education among family carers improves knowledge of pain management. This will equip informal carers to provide pain management within their homes confidently.
- Nurses and Midwifery Council of Malawi should review the curriculum for training nurses and midwives. They should incorporate pain education in the curriculum for the training of undergraduate nurses and nurse technicians in all colleges in Malawi. This will enable nurses to implement pain education when

they qualify as staff nurses. This will enable nurses to implement pain education when they qualify as staff nurses. Even though the pain education intervention did not test the effects of the intervention among student nurses, but as a way of implementation, training student nurses will enable them to put this into practice.

- HIV/AIDS and palliative care clinics should conduct further research into pain education to address the questions that have not been answered in the current study, for instance how effectively to implement pain education in routine care for HIV/AIDS patients. Such research will also help to answer the questions of how the pain education intervention worked, and which component is more feasible.

8.10 Conclusions

This study is unique because it is the first to investigate the effectiveness and feasibility of a nurse-led pain intervention among HIV/AIDS patients and their family carers in a resource poor country like Malawi. The study provides strong evidence to support the hypotheses that a simple nurse-led pain education intervention consisting of an information leaflet, augmented by face-to-face discussion and explanation for 30 minutes and a follow-up phone call after two weeks is effective in reducing the severity of pain, interference of pain, knowledge of pain management and quality of life among patients with HIV/AIDS. The study also supports the hypotheses that the intervention can be effective in improving the knowledge of pain management, motivation to provide care, and quality of life among family carers of patients with

HIV/AIDS.

The feasibility and acceptability of the intervention have been demonstrated by the enthusiasm and active support from health care workers from study settings, successful recruitment and low attrition among participants. This type of intervention could be replicated and implemented in other parts of the country and other countries in the sub-Saharan region.

Pain symptoms have become a major problem among people living with HIV/AIDS due to opportunistic infections and side effects of HIV treatment. Findings from this study have important implications for nurses and clinicians working in HIV/AIDS and palliative care clinics who are looking for effective interventions to manage pain symptoms which are highly prevalent among patients who receive HIV treatment.

More research is needed into the best ways to incorporate pain education into routine practice, the optimum time to evaluate the effects of the intervention. More research is needed to find out whether all the components of the pain education intervention were effective or not and which one was the most effective component.

The pain education intervention makes an important contribution to evidence for the development of practice in HIV/AIDS and palliative care clinics in Malawi and other countries in Sub-Saharan Africa and provides the basis for making recommendations to implement it in routine practice.

References

ABRAHA, I. & MONTEDORI, A. 2010. Modified intention to treat reporting in randomised controlled trials: systematic review. *BMJ: British Medical Journal,* 340.

ADDINGTON-HALL, J. M., BRUERA, E., HIGGINSON, I. J. & PAYNE, S. 2007. *Research methods in Palliative care,* Oxford, Oxford University Press.

AKOBENG, A. K. 2005a. Understanding randomised controlled trials. *Archives of Disease in Childhood,* 90**,** 840-844.

AKOBENG, A. K. 2005b. Understanding systematic reviews and meta-analysis. *Archives of Disease in Childhood,* 90**,** 845-848.

ANDERSON, K. O., MENDOZA, T. R., PAYNE, R., VALERO, V., PALOS, G. R., NAZARIO, A., RICHMAN, S. P., HURLEY, J., GNING, I., LYNCH, G. R., KALISH, D. & CLEELAND, C. S. 2004. Pain Education for Underserved Minority Cancer Patients: A Randomized Controlled Trial. *Journal of Clinical Oncology,* 22**,** 4918-4925.

ANDERSSON, G. B. J. 1999. Epidemiological features of chronic low-back pain. *The Lancet,* 354**,** 581-585.

AOUIZERAT, B. E., MIASKOWSKI, C. A., GAY, C., PORTILLO, C. J., COGGINS, T., DAVIS, H., PULLINGER, C. R. & LEE, K. A. 2010. Risk factors and symptoms associated with pain in HIV-infected adults. *Journal of the Association of Nurses in AIDS Care,* 21**,** 125-133.

AOUN, S., KRISTJANSON, L., HUDSON, P., CURROW, D. & ROSENBERG, J. 2005. The experience of supporting a dying relative: reflections of caregivers. *Progress in Palliative Care,* 13**,** 319 - 325.

APCA 2008. A Palliative Care Training Manual: Community Based Casegicers in Africa.

APCA 2012. Beating pain: A pocketguide for pain management in Africa. *In:* ASSOCIATION, A. P. C. (ed.) 2nd Edition ed.

ARMES, P. & ADDINGTON-HALL, J. 2003. Perspectives on symptom control in patients receiving community palliative care. *Palliative Medicine,* 17**,** 608-615.

ATTAL, N., CRUCCU, G., BARON, R., HAANPÄÄ, M., HANSSON, P., JENSEN, T. & NURMIKKO, T. 2010. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. *European Journal of Neurology,* 17**,** 1113-e88.

BALLANTYNE, J. C., COUSINS, M. J., GIAMBERARDINO, M. A., MCGRATH, P. A., SMITH, M. T., SOMMER, C., WITTINK, H. M., ENDRES, E., HAVERS, K. E. & BORAM, R. 2009. Cancer Pain Management in Developing Countries.

BECK, S. & AOCN 1999. Health policy, health services, and cancer pain management in the New South Africa. *J Pain Symp Manage,* 17**,** 16 - 26.

BECK, S. L. & FALKSON, G. 2001. Prevalence and management of cancer pain in South Africa. *Pain,* 94**,** 75-84.

BEEDHAM, H. & WILSON-BARNETT, J. 1995. HIV and AIDS care: consumers' views on needs and services. *Journal of Advanced Nursing,* 22**,** 677-686.

BENNETT, M. I., BAGNALL, A. M. & JOSE CLOSS, S. 2009. How effective are patient-based educational interventions in the management of cancer pain? Systematic review and meta-analysis. *Pain,* 143**,** 192-9.

BENNETT, M. I. & CLOSS, S. J. 2011. Methodological issues in nonpharmacological trials for chronic pain. *ANAESTHESIA, PAIN & INTENSIVE CARE,* 14**,** 126.

BOLLINGER, L., STOVER, J. & PALAMULENI, M. E. 2000. The economic impact of AIDS in Malawi.

BONOMI, A. E., WAGNER, E. H., GLASGOW, R. E. & VONKORFF, M. 2002. Assessment of chronic illness care (ACIC): a practical tool to measure quality improvement. *Health services research,* 37**,** 791-820.

BOON, H., RUITER, R. A., JAMES, S., VAN DEN BORNE, B., WILLIAMS, E. & REDDY, P. 2009a. Correlates of Grief Among Older Adults Caring for Children and Grandchildren as a Consequence of HIV and AIDS in South Africa. *Journal of Aging and Health*.

BOON, H., RUITER, R. A., JAMES, S., VAN DEN BORNE, B., WILLIAMS, E. & REDDY, P. 2009b. The impact of a community-based pilot health education intervention for older people as caregivers of orphaned and sick children as a result of HIV and AIDS in South Africa. *Journal of Cross-Cultural Gerontology,* 24**,** 373-89.

BORRELL-CARRIÓ, F., SUCHMAN, A. L. & EPSTEIN, R. M. 2004. The biopsychosocial model 25 years later: principles, practice, and scientific inquiry. *Annals of Family Medicine,* 2**,** 576-582.

BOTES, M. E. 2003. *Antiretroviral therapy: pharmacology. In Disease Review* Johnnic Publishing.

BRECHTL, J. R., BREITBART, W., GALIETTA, M., KRIVO, S. & ROSENFELD, B. 2001. The Use of Highly Active Antiretroviral Therapy (HAART) in Patients With Advanced HIV Infection: Impact on Medical, Palliative Care, and Quality of Life Outcomes. *Journal of Pain and Symptom Management,* 21**,** 41-51.

BREITBART, W. 1996a. Pain management and psychosocial issues in HIV and AIDS. *Caring,* 15**,** 26-35.

BREITBART, W. 1996b. Pain management and psychosocial issues in HIV and AIDS. *American Journal of Hospice & Palliative Care,* 13**,** 20-29.

BREITBART, W., MCDONALD, M., ROSENFELD, B., MONKMAN, N. & PASSIK, S. 1998. Fatigue in ambulatory AIDS patients. *Journal of Pain and Symptom Management,* 15**,** 159-67.

BREITBART, W., MCDONALD, M. V., ROSENFELD, B., PASSIK, S. D., HEWITT, D., THALER, H. & PORTENOY, R. K. 1996. Pain in ambulatory AIDS patients. I: Pain characteristics and medical correlates. *Pain,* 68**,** 315-321.

BRUNELLI, C., ZECCA, E., MARTINI, C., CAMPA, T., FAGNONI, E., BAGNASCO, M., LANATA, L. & CARACENI, A. 2010. Comparison of numerical and verbal rating scales to measure pain exacerbations in patients with chronic cancer pain. *Health and Quality of Life Outcomes,* 8**,** 42.

BULPITT, C. J. 1996. Randomised Controlled Clinical Trials. Boston: Kluwer Academic Publishers.

BUTTERS, E., HIGGINSON, I., GEORGE, R. & MCCARTHY, M. 1993. Palliative care for people with HIV/AIDS: views of patients, carers and providers. *AIDS Care,* 5**,** 105-116.

CAIRNS, G., FIELDHOUSE, R. & ALCORN, K. 2006. *HIV & AIDS reference manual,* London, Unwin Brothers.

CALLAGHAN, M., FORD, N. & SCHNEIDER, H. 2010. A systematic review of task-shift ing for HIV treatment and care in Africa. *Human Resources for Health,* 8.

CAMPBELL, J. N. & MITCHELL, M. J. 1996. *Pain Treatment Centers at a Crossroads: A Practical and Conceptual Reappraisal* Seattle, IASP Press.

CAMPBELL, L. C., CLAUW, D. J. & KEEFE, F. J. 2003. Persistent pain and depression: a biopsychosocial perspective. *Biological psychiatry,* 54**,** 399-409.

CAMPBELL, M., FITZPATRICK, R., HAINES, A., KINMONTH, A. L., SANDERCOCK, P., SPIEGELHALTER, D. & TYRER, P. 2000. Framework

for design and evaluation of complex interventions to improve health. *BMJ,* 321**,** 694-696.

CARACENI, A., CHERNY, N., FAINSINGER, R., KAASA, S., POULAIN, P., RADBRUCH, L. & DE CONNO, F. 2002a. Pain measurement tools and methods in clinical research in palliative care: recommendations of an expert working group of the European association of palliative care. *J Pain Symptom Manage,* 23**,** 239 - 255.

CARACENI, A., CHERNY, N., FAINSINGER, R., KAASA, S., POULAIN, P., RADBRUCH, L., DE CONNO, F. A. T. S. C. O. T. & NETWORK, E. R. 2002b. Pain Measurement Tools and Methods in Clinical Research in Palliative Care:

Recommendations of an Expert Working Group of the European Association of Palliative Care. *Journal of Pain and Symptom Management,* 23.

CARTWRIGHT, N. 2007. Are RCTs the Gold Standard? *BioSocieties,* 2**,** 11-20.

CASALE, M. & WHITESIDE, A. 2006. The Impact of HIV/AIDS on Poverty, Inequality and Economic Growth: IDRC working papers on Globilization, Growth and Poverty *In:* DIVISION, H. E. A. H. A. R. (ed.).

CATZ, S. & BALDERSON, B. 2014. Impact of a self-management telephone support programme for older people living with HIV on antiretroviral adherance and quality of life.

CENTRAL INTELLIGENCE AGENCY 2011. *The world factbook*.

CENTRAL INTELLIGENCE AGENCY 2013. The World Fact book.

CENTRE FOR DISEASE CONTROL 1993. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. *In:* HIV/AIDS, N. C. F. I. D. D. O. (ed.).

CENTRE FOR REVIEW AND DISSEMINATION. 2009. Systematic Reviews: CRD's Guidance for Undertaking Reviews in Health Care. Available: http://www.york.ac.uk/inst/crd/pdf/Systematic_Reviews.pdf.

CHAN, Y. H. 2003. Randomised Controlled Trials. *Singapore Medical Journal,* 44**,** 60-63.

CHESNEY, M. A., CHAMBERS, D. B., TAYLOR, J. M., JOHNSON, L. M. & FOLKMAN, S. 2003. Coping Effectiveness Training for Men Living With HIV: Results From a Randomized Clinical Trial Testing a Group-Based Intervention. *Psychosomatic Medicine,* 65**,** 1038-1046.

CHIMWAZA, A. F. & WATKINS, S. C. 2004. Giving care to people with symptoms of AIDS in rural sub-Saharan Africa. *AIDS Care,* 16**,** 795-807.

CHIOU, P.-Y., KUO, B. I.-T., LEE, M.-B., CHEN, Y.-M., CHUANG, P. & LIN, L.-C. 2006a. A programme of symptom management for improving quality of life and drug adherence in AIDS/HIV patients. *Journal of Advanced Nursing,* 55**,** 169-179.

CHIOU, P. Y., KUO, B. I., CHEN, Y. M., WU, S. I. & LIN, L. C. 2004. A program of symptom management for improving self-care for patients with HIV/AIDS. *AIDS Patient Care STDS,* 18**,** 539-47.

CHIOU, P. Y., KUO, B. I. T., LEE, M. B., CHEN, Y. M., CHUANG, P. & LIN, L. C. 2006b. A programme of symptom management for improving quality of life and drug adherence in AIDS/HIV patients. *Journal of advanced nursing,* 55**,** 169-179.

CLEELAND, C. S. 2009. The Brief Pain Inventory User Guide. Available: http://www.mdanderson.org/education-and-research/departments-programs-and-labs/departments-and-divisions/symptom-research/symptom-assessment-tools/BPI_UserGuide.pdf [Accessed 27/03/2014].

CLOTFELTER, C. E. 1999. The effect of an educational intervention on decreasing pain intensity in elderly people with cancer. *Oncol Nurs Forum,* 26**,** 27-33.

CLUCAS, C., HARDING, R., LAMPE, F., ANDERSON, J., JOHNSON, M., EDWARDS, S., FISHER, M. & SHERR, L. 2011. Doctor–patient concordance during HIV treatment switching decision-making. *HIV medicine,* 12**,** 87-96.

COHEN, C. A., COLANTONIO, A. & VERNICH, L. 2002. Positive aspects of caregiving: rounding out the caregiver experience. *International journal of geriatric psychiatry,* 17**,** 184-188.

COLLINS, J. A. & FAUSER, B. C. J. M. 2005. Balancing the strengths of systematic and narrative reviews. *Human Reproduction Update,* 11**,** 103-104.

COLLINS, K. & HARDING, R. 2007. Improving HIV management in Sub-Saharan Africa: how much palliative care is needed? *AIDS Care,* 19**,** 1304-1306.

COOK, D. J., MULROW, C. D. & HAYNES, R. 1997. Systematic reviews: Synthesis of best evidence for clinical decisions. *Annals of internal medicine* 126**,** 376-380.

COOK, D. J., SACKETT, D. L., SPITZER, W. O. & 1995. Methodologic guidelines for systematic reviews of randomized control trials in health care from the Potsdam Consultation on Meta-Analysis. *Journal of Clinical Epidemiology,* 48**,** 167-71.

CORMACK, D. 2000. *The research process in nursing,* Malden, Blackwell science.

COUGHLAN, M. 2003. Pain and Palliative Care for People Living with HIV/AIDS in Asia. *Journal of Pain and Palliative Care Pharmacotherapy,* 17**,** 91-104.

COX, S. & RICE, A. 2008. HIV and AIDS. *In:* WILSON, P. R., WATSON, P. J., HAYTHORNTHWAITE, J. A. & JENSEN, T. S. (eds.) *Clinical pain management: chronic pain.* London: Hodder and Stoughton.

CRAIG, P., DIEPPE, P., MACINTYRE, S., MICHIE, S., NAZARETH, I. & PETTICREW, M. 2008. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ,* 337**,** 979-983.

CRITICAL APPRAISAL SKILLS PROGRAMME. 2013. 11 questions to help you make sense of a trial. Available: http://www.caspinternational.org/mod_product/uploads/CASP%20Randomised%20Controlled%20Trial%20Checklist%2031.05.13.pdf [Accessed 25/02/2014].

DAVIES, H. I. O. & CROMBIE, I. K. 2001. What is a systematic review. *Evidence based medicine* [Online], 1. Available: http://www.medicine.ox.ac.uk/bandolier/painres/download/whatis/ebm.pdf [Accessed 25/12/2014].

DAY, S. J. & ALTMAN, D. G. 2000. Blinding in clinical trials and other studies. *BMJ,* 321**,** 504.

DDUNGU, H. 2011. Palliative care: what approaches are suitable in developing countries? *British journal of haematology,* 154**,** 728-735.

DE SILVA, M. J., BREUER, E., LEE, L., ASHER, L., CHOWDHARY, N., LUND, C. & PATEL, V. 2014. Theory of Change: a theory-driven approach to enhance the Medical Research Council's framework for complex interventions. *Trials,* 15**,** 267.

DE WIT, R., VAN DAM, F., ZANDBELT, L., VAN BUUREN, A., VAN DER HEIJDEN, K., LEENHOUTS, G. & LOONSTRA, S. 1997. A Pain Education Program for chronic cancer pain patients: follow-up results from a randomized controlled trial. *Pain,* 73**,** 55-69.

DEEKS, S. G., LEWIN, S. R. & HAVLIR, D. V. 2013. The end of AIDS: HIV infection as a chronic disease. *Lancet,* 382**,** 1525-33.

DEL BORGO, C., IZZI, I., CHIAROTTI, F., DEL FORNO, A., MOSCATI, A. M., CORNACCHIONE, E. & FANTONI, M. 2001. Multidimensional aspects of pain in HIV-infected individuals. *AIDS patient care and STDs,* 15**,** 95-102.

DEPARTMENT OF HEALTH 2008. Carers at the heart of 21st century families and communities: a caring system on your side, a life of your own.

DERDIARIAN, A. K. 1986. Informational Needs of Recently Diagnosed Cancer Patients. *Nursing Research September/October,* 35**,** 276-281.

DEROGATIS, L. R. & MELISARATOS, N. 1983. The Brief Symptom Inventory: an introductory report. *Psychol Med,* 13**,** 595-605.

DJULBEGOVIC, B. 2007. Articulating and responding to uncertainties in clinical research. *J Med Philos,* 32**,** 79 - 98.

DJULBEGOVIC, B., LACEVIC, M., CANTOR, A., FIELDS, K., BENNETT, C., ADAMS, J., KUDERER, N. & LYMAN, G. 2000. The uncertainty principle and industry-sponsored research. *Lancet,* 356**,** 635 - 638.

DOBALIAN, A., TSAO, J. C. & DUNCAN, R. P. 2004. *Pain and the use of outpatient services among persons with HIV: results from a nationally representative survey*, Medical care. 42 (2) (pp 129-138), 2004. Date of Publication: Feb 2004.

DOBKIN, P. L., PIHL, R. O. & BREAULT, C. 1991. Validation of the Derogatis Stress Profile using laboratory and real world data. *Psychother Psychosom,* 56**,** 185-96.

DOWSE, R., BARFORD, K. & BROWNE, S. 2014. Simple, illustrated medicines information improves ARV knowledge and patient self-efficacy in limited literacy South African HIV patients. *AIDS care***,** 1-7.

DUNN, L. 2002. Theories of learning. *Learning and teaching briefing papers series* [Online]. Available: http://www.brookes.ac.uk/services/ocsld/resources/briefing_papers/learning_theories.pdf [Accessed 23/10/2013].

DWORKIN, R. H., TURK, D. C., FARRAR, J. T., HAYTHORNTHWAITE, J. A., JENSEN, M. P., KATZ, N. P., KERNS, R. D., STUCKI, G., ALLEN, R. R. & BELLAMY, N. 2005a. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain; Pain*.

DWORKIN, R. H., TURK, D. C., FARRAR, J. T., HAYTHORNTHWAITE, J. A., JENSEN, M. P., KATZ, N. P., KERNS, R. D., STUCKI, G., ALLEN, R. R.,

BELLAMY, N., CARR, D. B., CHANDLER, J., COWAN, P., DIONNE, R., GALER, B. S., HERTZ, S., JADAD, A. R., KRAMER, L. D., MANNING, D. C., MARTIN, S., MCCORMICK, C. G., MCDERMOTT, M. P., MCGRATH, P., QUESSY, S., RAPPAPORT, B. A., ROBBINS, W., ROBINSON, J. P., ROTHMAN, M., ROYAL, M. A., SIMON, L., STAUFFER, J. W., STEIN, W., TOLLETT, J., WERNICKE, J., WITTER, J. & IMMPACT 2005b. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain,* 113**,** 9-19.

DWORKIN, R. H., TURK, D. C., WYRWICH, K. W., BEATON, D., CLEELAND, C. S., FARRAR, J. T., HAYTHORNTHWAITE, J. A., JENSEN, M. P., KERNS, R. D., ADER, D. N., BRANDENBURG, N., BURKE, L. B., CELLA, D., CHANDLER, J., COWAN, P., DIMITROVA, R., DIONNE, R., HERTZ, S., JADAD, A. R., KATZ, N. P., KEHLET, H., KRAMER, L. D., MANNING, D. C., MCCORMICK, C., MCDERMOTT, M. P., MCQUAY, H. J., PATEL, S., PORTER, L., QUESSY, S., RAPPAPORT, B. A., RAUSCHKOLB, C., REVICKI, D. A., ROTHMAN, M., SCHMADER, K. E., STACEY, B. R., STAUFFER, J. W., VON STEIN, T., WHITE, R. E., WITTER, J. & ZAVISIC, S. 2008. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. *J Pain,* 9**,** 105-21.

EBIRIM, L. N. & OTOKWALA, J. G. 2013. Inadequate pain relief in ambulatory patients with human immunodeficiency virus disease in Port Harcourt. *HIV/AIDS (Auckland, NZ),* 5**,** 199.

ELLENBERG, J. H. 2005. Intention to Treat Analysis. *Encyclopedia of Biostatistics.* John Wiley & Sons, Ltd.

ELLER, L. S., KIRKSEY, K. M., NICHOLAS, P. K., CORLESS, I. B., HOLZEMER, W. L., WANTLAND, D. J., WILLARD, S. S., ROBINSON, L., HAMILTON, M. J., SEFCIK, E. F., MOEZZI, S., MENDEZ, M. R., ROSA, M. & HUMAN, S. 2013. A randomized controlled trial of an HIV/AIDS Symptom Management Manual for depressive symptoms. *AIDS Care,* 25**,** 391-9.

ELZARRAD, M. K., ECKSTEIN, E. T. & GLASGOW, R. E. 2013. Applying chronic illness care, implementation science, and self-management support to HIV. *American journal of preventive medicine,* 44**,** S99-S107.

ENGEL, G. L. 1997. The need for a new medical model: a challenge for biomedicine *Science,* 196**,** 129-136.

ENS, C. D., CHOCHINOV, H. M., GWYTHER, E., MOSES, S., JACKSON, C., THOMPSON, G. & HARDING, R. 2011. Postgraduate palliative care education: Evaluation of a South African programme. *SAMJ: South African Medical Journal,* 101**,** 42-44.

EVANS, D. 2001. Systematic reviews of nursing research. *Intensive and critical care nursing* 17**,** 51-7.

EVANS, D. 2003. Hierarchy of evidence: a framework for ranking evidence evaluating healthcare interventions. *Journal of Clinical Nursing,* 12**,** 77-84.

EVANS, D. & PEARSON, A. 2001. Systematic reviews: gatekeepers of nursing knowledge. *Journal of clinical nursing* 10**,** 593-99.

FAN, A., KUO, H., KAO, D., MORISKY, D. & CHEN, Y. 2011. Quality of life and needs assessment on people living with HIV and AIDS in Malawi. *AIDS Care,* 23**,** 287-302.

FERRANS, C. E. & POWERS, M. J. 1985. Quality of life index: development and psychometric properties. *Advances in nursing science,* 8**,** 15-24.

FERRELL, B., RHINER, M. & RIVERA, L. M. 1993a. Development and Evaluation of the Family Pain Questionnaire. *Journal of Psychosocial Oncology,* 10**,** 21-35.

FERRELL, B. R., GRANT, M., CHAN, J., AHN, C. & FERRELL, B. A. The impact of cancer pain education on family caregivers of elderly patients. 1995. 1211.

FERRELL, B. R., RHINER, M. & FERRELL, B. A. 1993b. Development and implementation of a pain education program. *Cancer,* 72**,** 3426-3432.

FERRELL, B. R., TRAN, K., FERRELL, B. A. & AHN, C. 1994. Pain management for elderly patients with cancer at home. *Cancer,* 74**,** 2139-2146.

FLESCH, R. 1948. A new readability yardstick. *Journal of Applied Psychology,* 32**,** 221-233.

FOLEY, K. M. 1985. The Treatment of Cancer Pain. *New England Journal of Medicine,* 313**,** 84-95.

FRAMPTON, C. L. & HUGHES-WEBB, P. 2011. The measurement of Pain. *Clinical Oncology,* 23**,** 381-386.

FRANKEL, R. M., T.E., Q. & MCDANIEL, S. H. 2003. *The Biopsychosocial Approach: Past, Present, Future,* Rochester, NY, University of Rochester Press.

FRICH, L. M. & BORGBJERG, F. M. 2000. Pain and pain treatment in AIDS patients: a longitudinal study. *Journal of pain and symptom management,* 19**,** 339-347.

FULTON PICOT, S. J., YOUNGBLUT, J. A. & ZELLER, R. 1997. Development and testing of a measure of perceived caregiver rewards in adults. *Journal of Nursing Measurement,* 5**,** 33-52.

GHAEMI, S. N. 2009. The rise and fall of the biopsychosocial model. *The British Journal of Psychiatry,* 195**,** 3-4.

GIFFORD, A. L., LAURENT, D. D., GONZALES, V. M., CHESNEY, M. A. & LORIG, K. R. 1998. Pilot randomized trial of education to improve self-management skills of men with symptomatic HIV/AIDS. *Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology,* 18**,** 136-44.

GIFFORD, A. L. & SENGUPTA, S. 1999. Self-management health education for chronic HIV infection. *AIDS Care,* 11**,** 115-30.

GLARE, P. A. 2001. *Pain in patients with HIV infection: Issues for the new millennium*, European Journal of Pain. 5 (SUPPL. A) (pp 43-48), 2001. Date of Publication: 2001.

GLASGOW, R. E., MCKAY, H. G., PIETTE, J. D. & REYNOLDS, K. D. 2001. The RE-AIM framework for evaluating interventions: what can it tell us about approaches to chronic illness management? *Patient education and counseling,* 44**,** 119-127.

GLOBAL AIDS PROGRAMME. 2006. *keeping the promise? A study of progress made in implementing the UNGASS Declaration of commitment on HIV/AIDS in Malawi* [Online]. [Accessed Available at: http://www.panosaids.org/files/ungass_malawi_full.pdf , Accessed 19th November, 2011.

GOMES, B., CALANZANI, N., CURIALE, V., MCCRONE, P. & HIGGINSON, I. J. 2013. Effectiveness and cost-effectiveness of home palliative care services for adults with advanced illness and their caregivers. *Cochrane Database of Systematic Reviews,* 6**,** CD007760.

GOMES, B. & HIGGINSON, I. J. 2006. Factors influencing death at home in terminally ill patients with cancer: systematic review. *BMJ,* 332**,** 515-521.

GORDON-GAROFALO, V. L. & RUBIN, A. 2004. Evaluation of a Psychoeducational Group for Seronegative Partners and Spouses of Persons with HIV/AIDS. *Research on Social Work Practice,* 14**,** 14-26.

GORDON, D. B., L., J., MIASKOWSKI, C., MCCARBERG, B., TODD, K. H., PAICE, J. A., LIPMAN, A. G., BOOKBINDER, M., SANDERS, S. H., TURK, D. C. & CARR, D. B. 2005. American Pain Society Recommendations for Improving the Quality of Acute and Cancer Pain Management:

American Pain Society Quality of Care Task Force *Archives of Internal Medicine,* 165**,** 1574-1580.

GOUJARD, C. M. D., BERNARD, N. M. D., SOHIER, N. M. D. M. P. H., PEYRAMOND, D. M. D. P., LANCON, F. M., CHWALOW, J. P., ARNOULD, B. P. & DELFRAISSY, J.-F. M. D. P. 2003. Impact of a Patient Education Program on Adherence to HIV Medication: A Randomized Clinical Trial. *JAIDS Journal of Acquired Immune Deficiency Syndromes,* 34**,** 191-194.

GOVERNMENT OF MALAWI 2005. National Plan of Action for Orphans and other Vulnerable Children: 2005-2009. *In:* MALAWI., U. A. G. O. (ed.). Lilongwe.

GOVERNMENT OF MALAWI 2009. Malawi HIV and AIDS extended national action framework (NAF) 2010-12 Draft. *In:* CABINET, N. A. C. O. O. T. P. A. (ed.). Lilongwe.

GRAFF, M. J. L., VERNOOIJ-DASSEN, M. J. M., THIJSSEN, M., DEKKER, J., HOEFNAGELS, W. H. L. & RIKKERT, M. G. M. O. 2006. Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. *BMJ,* 333**,** 1196.

GRANDE, G. & EWING, G. 2008. Death at home unlikely if informal carers prefer otherwise: implications for policy. *Palliative Medicine,* 22**,** 971-972.

GRANDE, G., STAJDUHAR, K., AOUN, S., TOYE, C., FUNK, L., ADDINGTON-HALL, J., PAYNE, S. & TODD, C. 2009. Supporting lay carers in end of life care: current gaps and future priorities. *Palliative Medicine,* 23**,** 339 - 344.

GRANT, E., MURRAY, S., GRANT, A. & BROWN, J. 2003. A good death in rural Africa? Listening to patients and their families talk about care needs at the end of life. *J Pall Care,* 19**,** 3159 - 67.

GRANT, L., BROWN, J., LENG, M., BETTEGA, N. & MURRAY, S. 2011. Palliative care making a difference in rural Uganda, Kenya and Malawi: three rapid evaluation field studies. *BMC Palliative Care,* 10**,** 8.

GRAY, G. & BERGER, P. 2007. Pain in women with HIV/AIDS. *Pain,* 132 Suppl 1**,** S13-S21.

GRAY, G. E. & PINSON, L. A. 2003. Evidence-based medicine and psychiatric practice. *Psychiatric Quarterly,* 74**,** 387-399.

GREENER, R., JEFFERIS, K. & SIPHAMBE, H. 2000. The Impact of HIV/AIDS on Poverty and Inequality in Botswana. *South African Journal of Economics,* 68**,** 393-404.

GROND, S., ZECH, D., SCHUG, S. A., LYNCH, J. & LEHMANN, K. A. 1991. Validation of World Health Organization guidelines for cancer pain relief

during the last days and hours of life. *Journal of pain and symptom management,* 6**,** 411-422.

GWATKIN, D., BHUIYA, A. & VICTORIA, C. 2004. Making health system more equitable. 364**,** 1273-1280.

GWYTHER, L., BRENNAN, F. & HARDING, R. 2009. Advancing palliative care as a human right. *Journal of pain and symptom management,* 38**,** 767-774.

HAACKER, M. 2004. *The macroeconomics of HIV/AIDS* Washington DC.

HANSELL, P. S., HUGHES, C. B., CALIANDRO, G., RUSSO, P., BUDIN, W. C., HARTMAN, B. & HERNANDEZ, O. C. 1999. Boosting social support in caregivers of children with HIV/AIDS. *AIDS Patient Care & Stds,* 13**,** 297-302.

HARDING, R. & HIGGINSON, I. 2003. What is the best way to help caregivers in cancer and palliative care? A systematic literature review of interventions and their effectiveness. *Palliative Medicine,* 17**,** 63 - 74.

HARDING, R., HIGGINSON, I., LEAM, C., DONALDSON, N., PEARCE, A., GEORGE, R., ROBINSON, V. & TAYLOR, L. 2004a. Evaluation of a short term group of intervention for informal carers of patients attending a home palliative care service. *Journal of Pain and Symptom Management,* 27**,** 396 - 408.

HARDING, R., HIGGINSON, I. J., LEAM, C., DONALDSON, N., PEARCE, A., GEORGE, R., ROBINSON, V. & TAYLOR, L. 2004b. Evaluation of a short-term group intervention for informal carers of patients attending a home palliative care service. *Journal of Pain and Symptom Management,* 27**,** 396-408.

HARDING, R. & HIGGINSON, I. J. 2005. Palliative care in sub-Saharan Africa. *The Lancet,* 365**,** 1971-1977.

HARDING, R., KARUS, D., EASTERBROOK, P., RAVEIS, V. H., HIGGINSON, I. J. & MARCONI, K. 2005. Does palliative care improve outcomes for patients with HIV/AIDS? A systematic review of the evidence. *Sexually Transmitted Infections,* 81**,** 5-14.

HARDING, R., MOLLOY, T., EASTERBROOK, P., FRAME, K. & HIGGINSON, I. J. 2006. Is antiretroviral therapy associated with symptom prevalence and burden? *International Journal of STD & AIDS,* 17**,** 400-405.

HARDING, R., POWELL, R., DOWNING, J., CONNOR, S., MWANGI-POWELL, F., DEFILIPPI, K., CAMERON, S., GARANGANGA, E., KIKULE, E. & ALEXANDER, C. 2008. Generating an African palliative care evidence

base: The context, need, challenges and strategies. *J Pain Symp Manage,* 36**,** 304 - 309.

HARDING, R., POWELL, R. A., KIYANGE, F., DOWNING, J. & MWANGI-POWELL, F. 2010a. Provision of pain- and symptom-relieving drugs for HIV/AIDS in sub-Saharan Africa. *Journal of Pain and Symptom Management,* 40**,** 405-415.

HARDING, R., SELMAN, L., AGUPIO, G., DINAT, N., DOWNING, J., GWYTHER, L., MASHAO, T., MMOLEDI, K., MOLL, T. & MPANGA SEBUYIRA, L. 2010b. Validation of a core outcome measure for palliative care in Africa: the APCA African Palliative Outcome Scale. *Health and Quality of Life Outcomes,* 8**,** 10.

HARDING, R., SELMAN, L., POWELL, R. A., NAMISANGO, E., DOWNING, J., MERRIMAN, A., ALI, Z., GIKAARA, N., GWYTHER, L. & HIGGINSON, I. 2013. Research into palliative care in sub-Saharan Africa. *The Lancet Oncology,* 14**,** e183-e188.

HARDING, R., STEWART, K., MARCONI, K., O'NEILL, J. & HIGGINSON, I. 2003. Current HIV/AIDS end-of-life care in Sub-Saharan Africa: a survey of models, services, challenges and priorities. *BMC Public Health,* 3**,** 33.

HARRIES, A., HARGREAVES, N., GAUSI, F., KWANJANA, J. & SALANIPONI, F. 2001. High early death rate in tuberculosis patients in Malawi. *The International Journal of Tuberculosis and Lung Disease,* 5**,** 1000-1005.

HARRIES, A. D., LIBAMBA, E. & SCHOUTEN, E. J. 2006. Scaling up antiretroviral treatment in resource-poor settings. *Lancet* 367**,** 1870 – 1872.

HAWKER, G. A., MIAN, S., KENDZERSKA, T. & FRENCH, M. 2011. Measures of adult pain: Visual analog scale for pain (vas pain), numeric rating scale for pain (nrs pain), mcgill pain questionnaire (mpq), short-form mcgill pain questionnaire (sf-mpq), chronic pain grade scale (cpgs), short form-36 bodily pain scale (sf-36 bps), and measure of intermittent and constant osteoarthritis pain (icoap). *Arthritis care & research,* 63**,** S240-S252.

HEATH, K.V., MONTANER, J.S., BONDY, G., SINGER, J., O'SHAUGHNESSY, M.V., HOGG, R.S. 2003. Emerging drug toxicities of highly Active antiretroviral therapy for human immunodeficiency virus (HIV) infection. *Curr Drug Targets,* 4**,** 13-22.

HELP THE HOSPICES 2008. Carers services guide: setting up support services for carers of people with life limiting and terminal illnesses Help the hospices.

HEMRICH, G. & SCHNEIDER, B. 1997. HIV/AIDS as a Cross-Sectoral Issue for Technical Cooperation: focus on Agriculture and rural development.

HENRIKSSON, A., ÅRESTEDT, K., BENZEIN, E., TERNESTEDT, B.-M. & ANDERSHED, B. 2013. Effects of a support group programme for patients with life-threatening illness during ongoing palliative care. *Palliative Medicine,* 27**,** 257-264.

HEWITT, D. J., MCDONALD, M., PORTENOY, R. K., ROSENFELD, B., PASSIK, S. & BREITBART, W. 1997. Pain syndromes and etiologies in ambulatory AIDS patients. *Pain,* 70**,** 117-123.

HICKS, C., CURRIER, J., SAX, P., SHERER, R. & WANKE, C. 2003. Current management challenges in HIV: Tolerability of Antiretrovirals and metabolic complications *AIDS patient care and STDs,* 17**,** 221-233.

HIDER, S., EVANS, C., HILL, J. & HOUGHTON, S. 2011. Back pain. Arthritis Research UK.

HIGGINSON, I., WADE, A. & MCCARTHY, M. 1990. Palliative care: views of patients and their families. *British Medical Journal,* 301**,** 277-281.

HJERMSTAD, M., GIBBINS, J., HAUGEN, D., CARACENI, A., LOGE, J., KAASA, S. & ON BEHALF OF THE EPCRC, E. P. C. R. C. 2008. Pain assessment tools in palliative care: an urgent need for consensus. *Palliative Medicine,* 22**,** 895-903.

HJERMSTAD, M. J., FAYERS, P. M., HAUGEN, D. F., CARACENI, A., HANKS, G. W., LOGE, J. H., FAINSINGER, R., AASS, N. & KAASA, S. 2011. Studies Comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for Assessment of Pain Intensity in Adults: A Systematic Literature Review. *Journal of pain and symptom management,* 41**,** 1073-1093.

HJORLAND, B. 2011. Evidence based practice: An Analysis Based on the Philosophy of Science. *Journal of the American Society for Information Science and Technology,* 62**,** 1301-1310.

HØLEN, J. C., HJERMSTAD, M. J., LOGE, J. H., FAYERS, P. M., CARACENI, A., DE CONNO, F., FORBES, K., FÜRST, C. J., RADBRUCH, L. & KAASA, S. 2006. Pain Assessment Tools: Is the Content Appropriate for Use in Palliative Care? *Journal of Pain and Symptom Management,* 32**,** 567-580.

HOLLIS, S. & CAMPBELL, F. 1999. What is meant by intention-to-treat analysis? *BMJ,* 319**,** 670-674.

HOLZEMER, W., HENRY, S. & REILLY, C. 1998. Assessing and managing pain in AIDS care: the patient perspective. *Journal - Association of Nurses in AIDS Care,* 9**,** 22-30.

HOLZEMER, W., HUDSON, A., KIRKSEY, K., HAMILTON, M. & BAKKEN, S. 2001. The revised Sign and Symptom Check-list for HIV (SSC-HIVrev). *Journal of the Association of Nurses in AIDS Care,* 12**,** 60 - 70.

HUANG, K., OWINO, C., VREEMAN, R., HAGEMBE, M., NJUGUNA, F., STROTHER, R. & GRAMELSPACHER, G. 2012. Assessment of the face validity of two pain scales in Kenya: a validation study using cognitive interviewing. *BMC Palliative Care,* 11**,** 5.

HUDSON, A., KIRKSEY, K. & HOLZEMER, W. 2004. The Influence of Symptoms on Quality of Life among HIV-Infected Women. *Western Journal of Nursing Research,* 26**,** 9-23.

HUDSON, P. 2004. Positive aspects and challenges associated with caring for a dying relative at home. *International journal of palliative nursing,* 10**,** 58-65.

HUDSON, P., ARANDA, S. & HAYMAN-WHITE, K. 2005. A psycho-educational intervention for family caregivers of patients receiving palliative care: a randomised controlled trial. *Journal of Pain & Symptom Management,* 30**,** 329 - 341.

HUDSON, P. & PAYNE, S. 2009a. *Family Carers in Palliative Care: A guide for health and social care professionals,* Oxford, University Press.

HUDSON, P. & PAYNE, S. 2009b. The future of family caregiving: research, social policy and clinical practice. *Family Carers in Palliative Care: A guide for health and social care professionals***,** 277 - 303.

HUDSON, P., QUINN, K., KRISTJANSON, L., THOMAS, T., BRAITHWAITE, M., FISHER, J. & COCKAYNE, M. 2008. Evaluation of a psycho-educational group programme for family caregivers in home-based palliative care. *Palliative Medicine,* 22**,** 270-280.

HUDSON, P., REMEDIOS, C. & THOMAS, K. 2010. A systematic review of psychosocial interventions for family carers of palliative care patients. *BMC Palliative Care,* 9**,** 17.

HUDSON, P., THOMAS, K., QUINN, K., COCKAYNE, M. & BRAITHWAITE, M. 2009. Teaching family carers about home based palliative care: final results from a group education program. *Journal of Pain and Symptom Management,* 38**,** 299 - 308.

HUDSON, P. L., ARANDA, S. & HAYMAN-WHITE, K. 2005b. A psycho-educational intervention for family caregivers of patients receiving

palliative care: a randomized controlled trial. *J Pain Symptom Manage,* 30**,** 329-41.

HUGHES, A. 2004. Symptom Management in HIV-Infected Patients. *Journal of the Association of Nurses in AIDS Care,* 15**,** 7S-13S.

HUGHES, J., JELSMA, J., MACLEAN, E., DARDER, M. & TINISE, X. 2004. The health-related quality of life of people living with HIV/AIDS. *Disability and Rehabilitation,* 26**,** 371-6.

HUNT, J. 2009. *Family carers in resource- poor countries,* Oxford, University Press.

INOUYE, J., FLANNELLY, L. & FLANNELLY, K. J. 2000. Self-management training and quality of life of the individuals with HIV/AIDS. *The Hong Kong Nursing Journal,* 36**,** 5-13.

IVNIK, M. & JETT, M. Y. 2008. Creating written patient education materials. *CHEST Journal,* 133**,** 1038-1040.

JADAD, A. R. 1998. *Randomised controlled trials: a users guide,* London, BMJ Books.

JADAD, A. R. & BROWMAN, G. P. 1995. The WHO Analgesic Ladder for Cancer Pain Management. *JAMA: The Journal of the American Medical Association,* 274**,** 1870-1873.

JADAD, A. R. & ENKIN, M. W. 2007. *Randomised Controlled Trails: Questions, Answers and Musings*, Blackwell Publishing.

JAGWE, J. G. & BARNARD, D. 2002. The introduction of palliative care in Uganda. *Journal of Palliative Medicine,* 5**,** 159-163.

JONES, C. 1997. What HIV cost a tea estate in Malawi. *AIDS Analysis Africa,* 7**,** 5-7.

JONES, L. 2006. Childcare in poor urban settlements in Swaziland in an era of HIV/AIDS. *African Journal of AIDS Research,* 4**,** 161-171.

KAAYA, S. F., FAWZI, M. C., MBWAMBO, J. K., LEE, B., MSAMANGA, G. I. & FAWZI, W. 2002. Validity of the Hopkins Symptom Checklist-25 amongst HIV-positive pregnant women in Tanzania. *Acta Psychiatr Scand,* 106**,** 9-19.

KAMERMAN, P. R., WADLEY, A. L. & CHERRY, C. L. 2012. HIV-associated sensory neuropathy: risk factors and genetics. *Current pain and headache reports,* 16**,** 226-236.

KAPLAN, J. E., BENSON, C., HOLMES, K., BROOKS, J. T., PAU, A., MASUR, H., CONTROL, C. F. D., PREVENTION & AMERICA, H. M. A. O. T. I. D. S. O. 2009. Guidelines for prevention and treatment of opportunistic infections in HIV-infected adults and adolescents. *MMWR Recomm Rep,* 58**,** 1-207.

KAPLAN, J. E., HANSON, D., DWORKIN, M. S., FREDERICK, T., BERTOLLI, J., LINDEGREN, M. L., HOLMBERG, S. & JONES, J. L. 2000. Epidemiology of Human Immunodeficiency Virus-Associated Opportunistic Infections in the United States in the Era of Highly Active Antiretroviral Therapy. *Clinical Infectious Diseases,* 30**,** S5-S14.

KARUS, D., RAVEIS, V., ALEXANDER, C., HANNA, B., SELWYN, P., MARCONI, K. & HIGGINSON, I. 2005. Patient reports of symptoms and their treatment at three palliative care projects servicing individuals with HIV/AIDS. *Journal of Pain and Symptom Management,* 30**,** 408-17.

KAZANOWSKI, M. 2005. Family Caregivers' Medication Management of Symptoms in Patients With Cancer Near Death. *Journal of Hospice & Palliative Nursing,* 7**,** 174-181.

KELL, M. E. & WALLEY, J. D. 2009. Palliative care for HIV in the era of antiretroviral therapy availability: perspectives of nurses in Lesotho. *BMC Palliative Care,* 8**,** 11.

KELLER, S., BANN, C. M., DODD, S. L., SCHEIN, J., MENDOZA, T. R. & CLEELAND, C. S. 2004. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. *The Clinical Journal of Pain,* 20**,** 309.

KEMP, J., AITKEN, J. M., LEGRAND, S. & MWALE, B. 2003. Equity in ART? But the whole Health System is Inequitable: Equity in health sector responses to HIV/AIDS in Malawi. *Equinet.* Harare.

KHAN, K. S., KUNZ, R., KLEIJNEN, J. & ANTES, G. 2011. Systematic reviews to support evidence-based medicine: how to review and apply findings to health care research. London: Royal society of medicine press Ltd.

KIEBURTZ, K., SIMPSON, D., YIANNOUTSOS, C., MAX, M., HALL, C., ELLIS, R., MARRA, C., MCKENDALL, R., SINGER, E., DAL, P. G., CLIFFORD, D., TUCKER, T. & COHEN, B. 1998. A randomized trial of amitriptyline and mexiletine for painful neuropathy in HIV infection. AIDS Clinical Trial Group 242 Protocol Team. *Neurology,* 51**,** 1682-8.

KIKULE, E. 2003. A good death in Uganda: survey needs for palliative care for terminally ill people in urban areas. *BMJ,* 327**,** 192 - 194.

KIPP, W., TINDYEBWA, D., KARAMAGI, E. & RUBAALE, T. 2007a. How Much Should We Expect? Family Caregiving of AIDS Patients in Rural Uganda. *Journal of Transcultural Nursing,* 18**,** 358-365.

KIPP, W., TINDYEBWA, D., RUBAALE, T., KARAMAGI, E. & BAJENJA, E. 2007b. Family caregivers in rural Uganda: the hidden reality. *Health Care for Women International,* 28**,** 856-871.

KNOWLES, M. S. 1990. *The Adult Learner: a Neglected Species,* Houston, Gulf Publishing Company, Book Division.

KNOWLES, M. S., HOLTON III, E. F. & SWANSON, R. A. 2005. *The Adult Learner,* San Diego, Elsevier.

KUMWENDA, J. J. M., G. KAMPONDENI, S. VAN DAM AP, VAN LIESHOUT, L. ZIJLSTRA, E. E. 2005. Differential diagnosis of stroke in a setting of high HIV prevalence in Blantyre, Malawi. *Malawi Medical Journal* 17**,** 107-11.

LAGANA, L., CHEN, X.-H., KOOPMAN, C., CLASSEN, C., KIMERLING, R. & SPIEGAL, D. 2002. Depressive symptomatology in relation to emotional control and chronic pain in persons who are HIV positive. *Rehabilitation Psychology,* 47**,** 402.

LAI, Y.-H., GUO, S.-L., KEEFE, F. J., TSAI, S.-L., CHIEN, C.-C., SUNG, Y.-C. & CHEN, M.-L. 2004. Effects of brief pain education on hospitalized cancer patients with moderate to severe pain. *Supportive Care in Cancer,* 12**,** 645-652.

LARUE, F., FONTAINE, A. & COLLEAU, S. M. 1997. Underestimation and undertreatment of pain in HIV disease: multicentre study. *BMJ: British Medical Journal (International Edition),* 314**,** 23-28.

LASCHINGER, S. J., VAN MANEN, L., STEVENSON, T. & FOTHERGILL-BOURBONNAIS, F. Health care providers' and patients' perspectives on care in HIV ambulatory clinics across Ontario. *Journal of the Association of Nurses in AIDS Care,* 16**,** 37-48.

LAWSON, M., MAZENGERA, S., NOEL, T., MBAWA-NKHOMA, F. & 2008. Malawi Essential Health Service, Oxfam international.

LEBOVITS, A. H., LEFKOWITZ, M., MCCARTHY, D., SIMON, R., WILPON, H., JUNG, R. & FRIED, E. 1989. The prevalence and management of pain in patients with AIDS: a review of 134 cases. *The Clinical journal of pain,* 5**,** 245-248.

LECHNER, S. C., ANTONI, M. H., LYDSTON, D., LAPERRIERE, A., ISHII, M., DEVIEUX, J., STANLEY, H., IRONSON, G., SCHNEIDERMAN, N., BRONDOLO, E., TOBIN, J. N. & WEISS, S. 2003. Cognitive–behavioral

interventions improve quality of life in women with AIDS. *Journal of Psychosomatic Research,* 54**,** 253-261.

LEWITH, G. & LITTLE, P. 2007. *Randomized Controlled Trials,* London, Sage Publications.

LIN, C.-C., CHOU, P.-L., WU, S.-L., CHANG, Y.-C. & LAI, Y.-L. 2006. Long-term effectiveness of a patient and family pain education program on overcoming barriers to management of cancer pain. *Pain,* 122**,** 271-281.

LINDSEY, E., HIRSCHFELD, M., TLOU, S., LINDSEY, E., HIRSCHFELD, M. & TLOU, S. 2003. Home-based care in Botswana: experiences of older women and young girls. *Health Care for Women International,* 24**,** 486-501.

LONG, L. A., FOX, M. A. B., SANNE, I. A. C. & ROSEN, S. A. B. 2010. The high cost of second-line antiretroviral therapy for HIV/AIDS in South Africa. *AIDS,* 24**,** 915-919.

LORIG, K. R., SOBEL, D. S., STEWART, A. L., BROWN JR, B. W., BANDURA, A., RITTER, P., GONZALEZ, V. M., LAURENT, D. D. & HOLMAN, H. R. 1999. Evidence suggesting that a chronic disease self-management program can improve health status while reducing hospitalization: a randomized trial. *Medical care,* 37**,** 5-14.

LOVELL, M. R., FORDER, P. M., STOCKLER, M. R., BUTOW, P., BRIGANTI, E. M., CHYE, R., GOLDSTEIN, D. & BOYLE, F. M. 2010. A Randomized Controlled Trial of a Standardized Educational Intervention for Patients with Cancer Pain. *Journal of Pain and Symptom Management,* 40**,** 49-59.

MAKOAE, L., SEBONI, N., MOLOSIWA, K., MOLEKO, M., HUMAN, S., SUKATI, N. & HOLZEMER, W. 2005. The symptom experience of people living with HIV/AIDS in Southern Africa. *Journal of the Association of Nurses in AIDS Care,* 16**,** 22 - 32.

MAKOMBE, S., HOCHGESANG, M., JAHN, A., TWEYA, H., HEDT, B. & CHUKA, S. 2008a. Assessing the quality of data aggregated by antiretroviral treatment clinics in Malawi. *Bull World Health Organ,* 86**,** 310 - 4.

MAKOMBE, S., LIBAMBA, E., MHANGO, E., DE ASCURRA TECK, O., ABERLE-GRASSE, J. & HOCHGESANG, M. 2006. Who is accessing antiretroviral therapy during national scale-up in Malawi? *Trans R Soc Trop Med Hyg,* 100**,** 975 - 9.

MAKOMBE, S. D., JAHN, A. & TWEYA, H. E. A. 2008b. ART in the Malawi Police Force: Access to therapy and treatment outcomes. *Malawi Medical Journal* 20**,** 23-27.

MAKWIZA, I., NYIRENDA, L., BONGOLOLO, G., CHIMZIZI, R. & THEOBALD, S. 2009. Who has access to counselling and testing and anti-retroviral therapy in Malawi: an equity analysis. *International Journal of Health Equity,* 8.

MALAWI GOVERNMENT 2012a. 2012 Global AIDS Response: Progress Report; Malawi country report for 2010 and 2011.

MALAWI GOVERNMENT 2012b. How STEP UP helped integrate palliative care in Malawi.

MALAWI INSTITUTE OF MANAGEMENT 2008. Assessment of the impact of the public sector response to HIV and AIDS in the Malawi Public service.

MALTONI, M., SCARPI, E., MODONESI, C., PASSARDI, A., CALPONA, S., TURRIZIANI, A., SPERANZA, R., TASSINARI, D., MAGNANI, P., SACCANI, D., MONTANARI, L., ROUDNAS, B. & AMADORI, D. 2005. A validation study of the WHO analgesic ladder: a two-step vs three-step strategy. *Supportive Care in Cancer,* 13**,** 888-894.

MANAFA, O., MCAULIFFE, E., MASEKO, F., BOWIE, C., MACLACHLAN, M. & NORMAND, C. 2009. Retention of health workers in Malawi: perspectives of health workers and district management. *Human resources for health,* 7.

MANN, H. & DJULBEGOVIC, B. 2003. Clinical equipoise and the therapeutic misconception. *Hastings Cent Rep,* 33**,** 4.

MANSOOR, L. & DOWSE, R. 2007. Written medicines information for South African HIV/AIDS patients: does it enhance understanding of co-trimoxazole therapy? *Health Education Research,* 22**,** 37-48.

MANTZOUKAS, S. 2008. A review of evidence-based practice, nursing research and reflection: levelling the hierarchy. *Journal of Clinical Nursing,* 17**,** 214-223.

MARCUS, K. S., KERNS, R. D., ROSENFELD, B. & BREITBART, W. 2000. HIV/AIDS-related Pain as a Chronic Pain Condition: Implications of a Biopsychosocial Model for Comprehensive Assessment and Effective Management. *Pain Medicine,* 1**,** 260-273.

MARTIN, C., PEHRSSON, P., ÖSTERBERG, A., SÖNNERBORG, A. & HANSSON, P. 1999. Pain in ambulatory HIV-infected patients with and without intravenous drug use. *European Journal of Pain,* 3**,** 157-164.

MATEWELE, E. R. 2004. The impact of HIV/AIDS on human resources in the Malawi public sector. *15th International AIDS Conference.* Bangkok, Thailand.: International AIDS Society.

MATHENY, S. C. 2001. Clinical dilemmas in palliative care for HIV infection. *JRSM,* 94**,** 449-451.

MAY, C. 2006. A rational model for assessing and evaluating complex interventions in health care. *BMC health services research,* 6**,** 86.

MC CAFFERY, M. & BEEBE, A. 1989. *Pain: Clinical manual for nursing practice,* St Louis, C.V. Mosby.

MCCORMACK, J. P., LI, R., ZAROWNY, D. & SINGER, J. 1993. Inadequate treatment of pain in ambulatory HIV patients. *The Clinical journal of pain,* 9**,** 279-283.

MCCOY, D. 2003. Health Sector Response to HIV/AIDS and Treatment Access in Southern Africa: Addressing equity. Harare.

MCCUBBIN, M. A. & MCCUBBIN, H. I. 1991. Family stress theory and assessment: the resiliency model of family stress, adjustment and adaptation. *In:* MCCUBBIN, H. I. & THOMPSON, A. I. (eds.) *Family Assessment Inventories for Research and Practice.* Madison, Wis.: University of Wisconsin-Madison.

MEDICAL RESEARCH COUNCIL 2005. Medical Research Council position statement on research regulation and ethics.

MEEKER, M. A., FINNELL, D. & OTHMAN, A. K. 2011. Family Caregivers and Cancer Pain Management: A Review. *Journal of Family Nursing,* 17**,** 29-60.

MERRIMAN, A. 2006. Pain and symptom control in the Cancer and/or AIDS patient in Uganda and other African countries: A book for health professionals *Palliative medicine.* 6th Edition ed. Uganda: Hospice Africa Uganda

MERRIMAN, A. & HARDING, R. 2010. Pain Control in the African Context: the Ugandan introduction of affordable morphine to relieve suffering at the end of life. *Philosophy, Ethics, and Humanities in Medicine,* 5**,** 10.

MIASKOWSKI, C., DODD, M., WEST, C., SCHUMACHER, K., PAUL, S. M., TRIPATHY, D. & KOO, P. 2004. Randomized Clinical Trial of the Effectiveness of a Self-Care Intervention to Improve Cancer Pain Management. *Journal of Clinical Oncology,* 22**,** 1713-1720.

MIASKOWSKI, C., PENKO, J. M., GUZMAN, D., MATTSON, J. E., BANGSBERG, D. R. & KUSHEL, M. B. 2011. Occurrence and characteristics of chronic pain in a community-based cohort of indigent adults living with HIV infection. *The Journal of Pain,* 12**,** 1004-1016.

MICHIE, S. & ABRAHAM, C. 2004. Interventions to change health behaviours: evidence-based or evidence-inspired? *Psychology & Health,* 19**,** 29-49.

MILLARD, T., ELLIOTT, J. & GIRDLER, S. 2013. Self-Management Education Programs for People Living with HIV/AIDS: A Systematic Review. *AIDS patient care and STDs,* 27**,** 103-13.

MILLS, E., CHAN, A.-W., WU, P., VAIL, A., GUYATT, G. & ALTMAN, D. 2009. Design, analysis, and presentation of crossover trials. *Trials,* 10**,** 27.

MINISTRY OF HEALTH 1995. Health policy framework. Lilongwe.

MINISTRY OF HEALTH 1999. To the year 2020: a vision for the health sector in Malawi. Lilongwe.

MINISTRY OF HEALTH 2004. Treatment of AIDS: The two year plan to scale up Antiretroviral therapy in Malawi 2005-2005. *In:* HEALTH, M. O. (ed.). Lilongwe.

MINISTRY OF HEALTH 2005. Road Map for Accelerating the reduction of maternal and neonatal mortality and morbidity in Malawi. *In:* HEALTH, M. O. (ed.). Lilongwe, Malawi.

MINISTRY OF HEALTH 2006. Treatment of AIDS: Guidelines for the use of Antiretroviral therapy in Malawi. Lilongwe.

MINISTRY OF HEALTH 2008a. HIV and syphilis sero-survey and National HIV prevalence and AIDS estimates Report for 2007. *In:* HEALTH, M. O. (ed.). Lilongwe.

MINISTRY OF HEALTH 2008b. Introduction to Palliative Care: Health Professionals Training Manual. *In:* HEALTH, M. O. (ed.). Lilongwe, Malawi.

MINISTRY OF HEALTH 2009. National Palliative Care Guidelines. *In:* HEALTH, M. O. (ed.). Lilongwe.

MINISTRY OF HEALTH 2011a. Clinical Management of HIV in Children and Adults: Participant Work Book for Certification Course. *In:* HEALTH, M. O. (ed.). Lilongwe.

MINISTRY OF HEALTH 2011b. National Community Home-based care Policy and Guidelines,. *In:* HEALTH, M. O. (ed.). Lilongwe.

MINISTRY OF HEALTH 2014. Malawi Integrated guidelines for providong HIV services. *In:* AIDS, D. O. H. A. (ed.). Lilongwe.

MOHER, D., HOPEWELL, S., SCHULZ, K. F., MONTORI, V., GOTZSCHE, P. C., DEVEREAUX, P. J., ELBOURNE, D., EGGER, M. & ALTMAN, D. G. 2010.

CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ,* 340**,** c869.

MOHER, D. & OLKIN, I. 1995. Meta-analysis of Randomized Controlled Trials. *JAMA: The Journal of the American Medical Association,* 274**,** 1962-1964.

MONTORI, V. M. & GUYATT, G. H. 2001. Intention-to-treat principle. *Canadian Medical Association Journal,* 165**,** 1339-1341.

MORRISON, C. 1993. Delivery systems for the care of persons with HIV infection and AIDS. *The Nursing Clinics Of North America,* 28**,** 317-33.

MPHAHLELE, N., MITCHELL, D. & KAMERMAN, P. 2008. Validation of the Wisconsin Brief Pain Questionnaire in a multilingual South African population. *Journal of pain and symptom management,* 36**,** 396-412.

MPHANDE, H. 2014. Shortage of nurses hit Malawi: has only 25% of the required numbers. *Nyasa Times*.

MTIKA, M. 1998. Illness, deaths, and social obligations: peasant food security in the context of AIDS in Malawi. *Int Conf AIDS* 12, 472

MULROW, C., COOK, D. & DAVIDOFF, F. 1997. Systematic reviews: critical links in the great chain of evidence. *Annals of internal medicine,* 126**,** 389-91.

MUNTHALI, C., TAEGTMEYER, M., GARNER, P. G., LALLOO, D. G., SQUIRE, S. B., CORBETT, E. L., FORD, N. & MACPHERSON, P. 2014. Diagnostic accuracy of the WHO clinical staging system for defining eligibility for ART in sub-Saharan Africa: a systematic review and meta-analysis. *Journal of the International AIDS Society,* 17.

MURPHY, J., GAMBLE, G. & SHARPE, N. 1994. Readability of subject information leaflets for medical research. *The New Zealand medical journal,* 107**,** 509-510.

MUTUME, G. 2001. Malawi battles AIDS orphan nightmare: communities struggle to provide care with few resources. *African recovery* 15**,** 17-20.

MWINGIRA, B. & DOWSE, R. 2007. Development of written information for antiretroviral therapy: comprehension in a Tanzanian population. *Pharmacy World & Science,* 29**,** 173-182.

MWINITUO, P. P. & MILL, J. E. 2006. Stigma Associated With Ghanaian Caregivers of AIDS Patients. *Western Journal of Nursing Research,* 28**,** 369-382.

NAIR, S., THEOPHIN, R., PRARTHANA, S. & HARRISON, P. 2009. Prevalence of pain in patients with HIV/AIDS: A cross-sectional survey in a south Indian state. *Indian Journal of Palliative Care,* 15**,** 67-70.

NAMISANGO, E., HARDING, R., ATUHAIRE, L., DDUNGU, H., KATABIRA, E., MUWANIKA, F. R. & POWELL, R. A. 2012. Pain among ambulatory HIV/AIDS patients: multicenter study of prevalence, intensity, associated factors, and effect. *The Journal of Pain,* 13**,** 704-713.

NARASIMOOLOO, C., NAIDOO, S. & GAEDE, B. 2011. Adequacy of pain management in HIV-positive patients. *South African Family Practice,* 53.

NATIONAL AIDS COMMISSION 2003. National HIV/AIDS Policy: A call for Renewed Action. Lilongwe, Malawi.

NATIONAL STATISTICAL OFFICE 2003. Statistical year book, 2003. *In:* OFFICE, N. S. (ed.). Zomba, Malawi.

NDABA-MBATA, R. D. & SELOILWE, E. S. 2000. Home-based care of the terminally ill in Botswana: knowledge and perceptions. *International Nursing Review,* 47**,** 218-223.

NEWSHAN, G. 1995. Pain management in HIV and AIDS. *Gmhc Treatment Issues: the Gay Men's Health Crisis Newsletter of Experimental AIDS Therapies,* 9**,** 5, 10-2.

NEWSHAN, G. 1997. Pain in human immunodeficiency virus disease. *Seminars in Oncology Nursing,* 13**,** 36-41.

NEWSHAN, G. & SHERMAN, D. W. 1999. Palliative care: pain and symptom management in persons with HIV/AIDS. *Nursing Clinics of North America,* 34**,** 131-45.

NICHOLAS, P. K., VOSS, J., WANTLAND, D., LINDGREN, T., HUANG, E., HOLZEMER, W. L., CUCA, Y., MOEZZI, S., PORTILLO, C., WILLARD, S., ARUDO, J., KIRKSEY, K., CORLESS, I. B., ROSA, M. E., ROBINSON, L., HAMILTON, M. J., SEFCIK, E., HUMAN, S., RIVERO-MENDEZ, M., MARYLAND, M., NOKES, K. M., ELLER, L., KEMPPAINEN, J., DAWSON-ROSE, C., BRION, J. M., BUNCH, E. H., SHANNON, M., NICHOLAS, T. P., VIAMONTE-ROS, A. & BAIN, C. A. 2010. Prevalence, self-care behaviors, and self-care activities for peripheral neuropathy symptoms of HIV/AIDS. *Nursing & Health Sciences,* 12**,** 119-26.

NKHOMA, K., SEYMOUR, J. & ARTHUR, A. 2013. An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: study protocol for a randomised controlled trial. *Trials,* 14**,** 216.

NOBLE, B., CLARK, D., MELDRUM, M., TEN HAVE, H., SEYMOUR, J., WINSLOW, M. & PAZ, S. 2005. The measurement of pain, 1945–2000. *Journal of Pain and Symptom Management,* 29**,** 14-21.

NORSE, D. 1992. Impact of AIDS on food production in East Africa. *AIDS Analysis Africa* 2.

NORTHOUSE, L. L., KATAPODI, M. C., SONG, L., ZHANG, L. & MOOD, D. W. 2010. Interventions with Family Caregivers of Cancer Patients: Meta-Analysis of Randomized Trials. *CA: A Cancer Journal for Clinicians,* 60**,** 317-339.

NORVAL, D. 2004. Symptoms and sites of pain experienced by AIDS patients. *S Afr Med J,* 94**,** 450 - 454.

O'NEIL, M., JARRAH, Z., NKOSI, L., COLLINS, D., PERRY, C., JACKSON, J., KUCHANDE, H. & MLAMBALA, A. 2010. *Evaluation of Malawi's Emergency Human Resources Programme* [Online]. Available: http://www.msh.org/news-bureau/upload/Evaluation-of-Malawi-s-Emergency-Human-Resources-Programme.pdf [Accessed 01/12/11.

OGDEN, J., ESIM, S. & GROWN, C. 2006. Expanding the care continuum for HIV/AIDS: bringing carers into focus. *Health Policy Plan,* 21**,** 333-42.

OLDENMENGER, W. H., SILLEVIS SMITT, P. A. E., VAN MONTFORT, C. A. G. M., DE RAAF, P. J. & VAN DER RIJT, C. C. D. 2011. A combined pain consultation and pain education program decreases average and current pain and decreases interference in daily life by pain in oncology outpatients: A randomized controlled trial. *PAIN,* 152**,** 2632-2639.

OLDHAM, L. & KRISTJANSON, L. J. 2004. Development of a pain management programme for family carers of advanced cancer patients. *International Journal of Palliative Nursing,* 10**,** 91-99.

PAICE, J. A., FERRELL, B., COYLE, N., COYNE, P. & SMITH, T. 2010. Living and Dying in East Africa. *Clinical journal of oncology nursing,* 14**,** 161-166.

PAKENHAM, K. I., DADDS, M. R. & LENNON, H. V. 2002. The efficacy of a psychosocial intervention for HIV/AIDS caregiving dyads and individual caregivers: a controlled treatment outcome study. *AIDS Care,* 14**,** 731-50.

PAREDES, R. & CLOTET, B. 2003. New antiretroviral drugs and approaches to HIV treatment. *AIDS***,** S85-S96.

PARKER, R., STEIN, D. J. & JELSMA, J. 2014. Pain in people living with HIV/AIDS: a systematic review. *J Int AIDS Soc,* 17**,** 18719.

PAYNE, S. S., P. AND DEAN, S. 1999. Identifying the concerns of informal carers in palliative care. *Palliative Medicine,* 13**,** 37-44.

PELTZER, K. & PHASWANA-MAFUYA, N. 2008. The symptom experience of people living with HIV and AIDS in the Eastern Cape, South Africa. *BMC health services research,* 8**,** 271.

PELTZER, K., PREEZ, N., RAMLAGAN, S. & FOMUNDAM, H. 2008. Use of traditional complementary and alternative medicine for HIV patients in KwaZulu-Natal, South Africa. *BMC Public Health,* 8**,** 255.

PELTZER, K., RAMLAGAN, S., JONES, D., WEISS, S. M., FOMUNDAM, H. & CHANETSA, L. 2012. Efficacy of a lay health worker led group antiretroviral medication adherence training among non-adherent HIV-positive patients in KwaZulu-Natal, South Africa: Results from a randomized trial. *SAHARA-J: Journal of Social Aspects of HIV/AIDS,* 9**,** 218-226.

PETTICREW, M. 2011. When are complex interventions 'complex'? When are simple interventions 'simple'? *The European Journal of Public Health,* 21**,** 397-398.

PHILLIPS, T. J., CHERRY, C. L., COX, S., MARSHALL, S. J. & RICE, A. S. 2010. Pharmacological treatment of painful HIV-associated sensory neuropathy: a systematic review and meta-analysis of randomised controlled trials. *PLoS One,* 5**,** e14433.

PHIRI, S. & WEBB, D. 2002. The Impact of HIV/AIDS on Orphans and Programme and Policy Responses.

PICOT, S. J., DEBANNE, S. M., NAMAZI, K. H. & WYKLE, M. L. 1997. Religiosity and Perceived Rewards of Black and White Caregivers. *The Gerontologist,* 37**,** 89-101.

POCOCK, S. J. 1983. *Clinical Trials: A Practical Approach,* Chichester, John Wiley and sons.

POLIT, D. F. & BECK, C. T. 2008. *Nursing Research: Generating and Assessing Evidence for Nursing Practice,* Philadelphia, Wolters Kluwer/Lippincott Williams and Wilkins.

POLIT, H. 2006. *Nursing research: principles and methods,* Philadelphia, J.B. Lippincott.

POMEROY, E. C., RUBIN, A. & WALKER, R. J. 1995. Effectiveness of a psychoeducational and task-centered group intervention for family members of people with AIDS. *Social Work Research,* 19**,** 142-152.

POWELL, R. A., DOWNING, J., HARDING, R., MWANGI-POWELL, F. & CONNOR, S. 2007. Development of the APCA African Palliative Outcome Scale. *Journal of Pain and Symptom Management,* 33**,** 229-232.

RABINSTEIN, A. A. 2003. Srtoke in HIV-infected patients: a clinical perspective *Cerebrovascular diseases,* 15**,** 37-44.

RABOW, M. W., HAUSER, J. M. & ADAMS, J. 2004. Supporting Family Caregivers at the End of Life. *JAMA: The Journal of the American Medical Association,* 291**,** 483-491.

RABSON, E., ANSELL, N., VAN BLERK, L., CHIPETA, L. & HAJDU, F. 2007. AIDS and food insecurity: New variant famine in Malawi. *MMJ,* 19**,** 136-7.

RAJESH, R., VIDYASAGAR, S., MURALIDHAR VARMA, D., GUDDATTU, V. & HAMEED, A. 2013. Evaluating the Impact of Educational Interventions on Use of Highly Active Antiretroviral Therapy and Adherence Behavior in Indian Human Immunodeficiency Virus Positive Patients: Prospective Randomized Controlled Study. *Journal of AIDS & Clinical Research*.

RENDERS, C. M., VALK, G. D., GRIFFIN, S. J., WAGNER, E. H., EIJK VAN, J. T. & ASSENDELFT, W. J. 2001. Interventions to improve the management of diabetes in primary care, outpatient, and community settings: a systematic review. *Diabetes Care,* 24**,** 1821-33.

RICHARDSON, J. L., HEIKES, B., KARIM, R., WEBER, K., ANASTOS, K. & YOUNG, M. 2009. *Experience of pain among women with advanced HIV disease*, AIDS Patient Care and STDs. 23 (7) (pp 503-511), 2009. Date of Publication: 01 Jul 2009.

ROGERS, A. & HORROCKS, N. 2010. *Teaching Adults,* Berkshire, McGraw Hill Open University Press.

ROLAND, M. & TORGERSON, D. 1998a. What outcomes should be measured? *BMJ,* 317**,** 1075-1080.

ROLAND, M. & TORGERSON, D. J. 1998b. What are pragmatic trials? *BMJ,* 316**,** 285.

ROSEN, S., KETLHAPILE, M., SANNE, I. & DESILVA, M. B. 2008. Differences in normal activities, job performance and symptom prevalence between patients not yet on antiretroviral therapy and patients initiating therapy in South Africa. *Aids,* 22**,** S131-S139.

ROSENFELD, B., BREITBART, W., MCDONALD, M. V., PASSIK, S. D., THALER, H. & PORTENOY, R. K. 1996. Pain in ambulatory AIDS patients. II: Impact of pain on psychological functioning and quality of life. *Pain,* 68**,** 323-328.

ROTHERAM-BORUS, M. J. 2000. Variations in perceived pain associated with emotional distress and social identity in AIDS. *AIDS patient care and STDs,* 14**,** 659-665.

ROTHERAM-BORUS, M. J., LEE, M. B., GWADZ, M. & DRAIMIN, B. 2001. An intervention for parents with AIDS and their adolescent children. *American Journal of Public Health,* 91**,** 1294-1302.

ROUSH, S. 2008. Randomized controlled trials and the flow of information: comment on Cartwright. *Springer,* 143**,** 137-145.

ROWAN, D. & KABWIRA, D. B. 2009. Empowering HIV/AIDS Orphans Through Teaching Vocational Trades: A SWOT Analysis of a Community-Based Orphan Training Program in Malawi. *Journal of global social work practice,* 2.

SABIN, C. A. 2002. The changing clinical epidemiology of AIDS in the highly active antiretroviral therapy era. *AIDS,* 16.

SACAJIU, G., RAVEIS, V. H. & SELWYN, P. 2009. Patients and family care givers' experiences around highly active antiretroviral therapy (HAART). *AIDS Care,* 21**,** 1528-36.

SACKTOR, N. 2002. The epidemiology of human immunodeficiency virus-associated neurological disease in the era of highly active antiretroviral therapy. *Journal Of Neurovirology,* 8 Suppl 2**,** 115-121.

SAKS, M. & ALLSOP, J. 2007. *Researching health: qualitative, quantitative and mixed methods,* London, Sage Publications.

SALINAS, G. & HAACKER, M. 2006. HIV/AIDS: The Imapct on Poverty and Inequality. *In:* FUND, I. M. (ed.).

SAMARKOS, M. G. 2006. The pholosophy of Evidence-based Medicine. *Hospital chronicles,* 1**,** 27-35.

SAUNDERS, C. & SYKES, N. 1993. *The management of terminal malignant disease,* London, E. Arnold.

SCANDLYN, J. 2000. When AIDS became a chronic disease. *West J Med,* 172**,** 130-3.

SCHULZ, K. F., CHALMERS, I., HAYES, R. J. & ALTMAN, D. G. 1995. Empirical evidence of bias: dimensions of methodological quality associated with estimates of treatment effects in controlled trials. *Journal of American Medical Association,* 273**,** 408-412.

SEDGWICK, P. 2011. Analysis by per protocol. *BMJ,* 342.

SEDGWICK, P. 2012. *Cluster randomised controlled trials*.

SEDGWICK, P. 2013. What is per protocol analysis? *BMJ: British Medical Journal,* 346.

SELMAN, L., SIEGERT, R. J., HIGGINSON, I. J., AGUPIO, G., DINAT, N., DOWNING, J., GWYTHER, L., MASHAO, T., MMOLEDI, K. & MOLL, T. 2012. The "Spirit 8" successfully captured spiritual well-being in African palliative care: factor and Rasch analysis. *Journal of clinical epidemiology,* 65**,** 434-443.

SELMAN, L., SPECK, P., GYSELS, M., AGUPIO, G., DINAT, N., DOWNING, J., GWYTHER, L., MASHAO, T., MMOLEDI, K., MOLL, T., SEBUYIRA, L. M., IKIN, B., HIGGINSON, I. J. & HARDING, R. 2013. 'Peace' and 'life worthwhile' as measures of spiritual well-being in African palliative care: a mixed-methods study. *Health Qual Life Outcomes,* 11**,** 94.

SELWYN, P. A. 2005. *Sexually Transmitted Infections,* 81**,** 2.

SEPULVEDA, C., HABIYAMBERE, V., AMANDUA, J., BOROK, M., KIKULE, E., MUDANGA, B., NGOMA, T. & SOLOMON, B. 2003. Quality care at the end of life in Africa. *British Medical Journal,* 327**,** 209-13.

SEPULVEDA, C., MARLIN, A., YOSHIDA, T. & ULLRICH, A. 2002. Palliative Care: the World Health Organization's global perspective. *J Pain Symptom Manage,* 24**,** 91 - 96.

SHERR, L., CLUCAS, C., HARDING, R., SIBLEY, E. & CATALAN, J. 2011. HIV and depression–a systematic review of interventions. *Psychology, Health & Medicine,* 16**,** 493-527.

SHERR, L., LAMPE, F., NORWOOD, S., LEAKE-DATE, H., FISHER, M., EDWARDS, S., ARTHUR, G., ANDERSON, J., ZETLER, S., JOHNSON, M. & HARDING, R. 2007. Successive switching of antiretroviral therapy is associated with high psychological and physical burden. *International Journal of STD & AIDS,* 18**,** 700-704.

SHLAY, J. C., CHALONER, K., MAX, M. B., FLAWS, B., REICHELDERFER, P., WENTWORTH, D., HILLMAN, S., BRIZZ, B., COHN, D. L. & AIDS, T. B. C. P. F. C. R. O. 1998. Acupuncture and amitriptyline for pain due to HIV-related peripheral neuropathy: a randomized controlled trial. *Jama,* 280**,** 1590-1595.

SIBALE, B. & NTHAMBI, T. 2008. Mid-term review of the National plan of action for orphaned and other vulnerable children: Draft report.

SIBBALD, B. & ROBERTS, C. 1998. *Understanding controlled trials Crossover trials*.

SIBBALD, B. & ROLAND, M. 1998. Understanding controlled trials: Why are randomised controlled trials important? *BMJ,* 316**,** 201.

SIGN 2009. Cancer pain: Booklet for patients and carers. 2-29.

SIMMS, V., GIKAARA, N., MUNENE, G., ATIENO, M., KATAIKE, J., NSUBUGA, C., BANGA, G., NAMISANGO, E., PENFOLD, S., FAYERS, P., POWELL, R. A., HIGGINSON, I. J. & HARDING, R. 2013. Multidimensional patient-reported problems within two weeks of HIV diagnosis in East Africa: a multicentre observational study. *PLoS One,* 8**,** e57203.

SIMPSON, D. M., SCHIFITTO, G., CLIFFORD, D., MURPHY, T., DURSO-DE CRUZ, E., GLUE, P., WHALEN, E., EMIR, B., SCOTT, G. & FREEMAN, R. 2010. Pregabalin for painful HIV neuropathy A randomized, double-blind, placebo-controlled trial. *Neurology,* 74**,** 413-420.

SMALBRUGGE, M., JONGENELIS, L., POT, A., BEEKMAN, A. & EEFSTING, J. 2007. Pain among nursing home patients in the Netherlands: prevalence, course, clinical correlates, recognition and analgesic treatment - an observational cohort study. *BMC Geriatrics,* 7**,** 3.

SMITH FAWZI, M. C., EUSTACHE, E., OSWALD, C., LOUIS, E., SURKAN, P. J., SCANLAN, F., HOOK, S., MANCUSO, A. & MUKHERJEE, J. S. 2012. Psychosocial support intervention for HIV-affected families in Haiti: implications for programs and policies for orphans and vulnerable children. *Social Science & Medicine,* 74**,** 1494-503.

SOLANO, J. P., GOMES, B. & HIGGINSON, I. J. 2006. A Comparison of Symptom Prevalence in Far Advanced Cancer, AIDS, Heart Disease, Chronic Obstructive Pulmonary Disease and Renal Disease. *Journal of Pain and Symptom Management,* 31**,** 58-69.

SPECTOR, T. D. & THOMPSON, S. G. 1991. The potential and limitations for meta-analysis. *J Epidermiol community health,* 45**,** 89-92.

SPIELBERGER, C. D., GORSUCH, R. L., LUSHENE, R., VAGG, P. R. & JACOBS, G. A. 1983. *Manual for the State-Trait Anxiety Inventory,* Palo Alto, CA, Consulting Psychologists Press, Inc.

SPROSS, J. A., MCGUIRE, D. B. & SCHMITT, R. M. Oncology Nursing Society Position Paper on Cancer Pain. Part I. Oncology nursing forum, 1990. 595.

STAJDUHAR, K., FUNK, L., TOYE , C., GRANDE, G., AOUN, S. & TODD, C. 2010. Part 1: Home-based family caregiving at the end of life: a comprehensive review of published quantitative research (1998-2008). *Palliative Medicine,* 24**,** 573-593.

STATACORP 2011. Stata Statistical Software: Release 12. College Station, TX: StataCorp LP. College Station, TX.

STEEDS, C. E. 2009. The anatomy and physiology of pain. 27**,** 507-511.

STJERNSWARD, J. 2002. Uganda: initiating a government public health approach to pain relief and palliative care. *Journal of Pain & Symptom Management,* 24**,** 257 - 264.

STJERNSWÄRD, J., FOLEY, K. M. & FERRIS, F. D. 2007. The public health strategy for palliative care. *Journal of pain and symptom management,* 33**,** 486-493.

STOLBERG, H. O., NORMAN, G. & TROP, I. 2004. Randomized Controlled Trials. *American Journal of Roentgenology,* 183**,** 1539-1544.

STOLTZ, P., UDÉN, G. & WILLMAN, A. 2004. Support for family carers who care for an elderly person at home–a systematic literature review. *Scandinavian journal of caring sciences,* 18**,** 111-119.

SUBBARAMAN, R., CHAGUTURU, S. K., MAYER, K. H., FLANIGAN, T. P. & KUMARASAMY, N. 2007. Adverse Effects of Highly Active Antiretroviral Therapy in Developing Countries. *Clinical Infectious Diseases,* 45**,** 1093-1101.

SUKATI, N. A., MNDEBELE, S. C., MAKOA, E. T., RAMUKUMBA, T. S., MAKOAE, L. N., SEBONI, N. M., HUMAN, S. & HOLZEMER, W. L. 2005. *HIV/AIDS symptom management in Southern Africa*, Journal of Pain and Symptom Management. 29 (2) (pp 185-192), 2005. Date of Publication: Feb 2005.

SWARTZ, L. & DICK, J. 2002. Managing chronic diseases in less developed countries: healthy teamworking and patient partnership are just as important as adequate funding. *BMJ: British Medical Journal,* 325**,** 914.

TAPSFIELD, J. B. & JANE BATES, M. 2011. Hospital based palliative care in sub-Saharan Africa; a six month review from Malawi. *BMC Palliative Care,* 10**,** 12-12.

THE DAILY TIMES 2008. AIDS Scourge: four nurses die monthly.

THIELEMANN, P. 2000. Educational needs of home caregivers of terminally ill patients: Literature review. *American Journal of Hospice and Palliative Medicine,* 17**,** 253-257.

TILDEN, V. P., NELSON, C. A. & MAY, B. A. 1990. The IPR inventory: development and psychometric characteristics. *Nurs Res,* 39**,** 337-43.

TORGERSON, D. J. 2001. Contamination in trials: is cluster randomisation the answer? *BMJ: British Medical Journal,* 322**,** 355.

TURK, D. C., DWORKIN, R. H., ALLEN, R. R., BELLAMY, N., BRANDENBURG, N., CARR, D. B., CLEELAND, C., DIONNE, R., FARRAR, J. T. & GALER, B. S. 2003. Core outcome domains for chronic pain clinical trials: IMMPACT recommendations. *Pain,* 106**,** 337-345.

UNAIDS 2006. Impact of HIV/AIDS on people and societies

UNAIDS 2010. UNAIDS report on the global AIDS epidemic.

UNAIDS 2012. Global Report: UNAIDS Report on the Global AIDS Epidemic 2012.

UNAIDS. 2013. *UNAIDS report on the global AIDS epidemic 2013* [Online]. Available: http://www.unaids.org/en/resources/campaigns/globalreport2013/factsheet/.

UNITED NATIONS DEVELOPMENT PROGRAMME 2002. The impact of HIV/AIDS on human resources in the Malawi Public sector.

UNRUH, A. M. 1996. Gender variations in clinical pain experience. *Pain,* 65**,** 123-167.

UWIMANA, J. & STRUTHERS, P. 2007. Met and unmet palliative care needs of people living with HIV/AIDS in Rwanda. *SAHARA J: Journal of Social Aspects of HIV/AIDS Research Alliance,* 4**,** 575-85.

UWIMANA, J. & STRUTHERS, R. 2008. Assessment of palliative care needs for people living with HIV/AIDS in Rwanda. *Progress in Palliative Care,* 16**,** 119-28.

VALLERAND, A. H. & POLOMANO, R. C. 2000. The relationship of gender to pain. *Pain Management Nursing,* 1**,** 8-15.

VAN AS, M., MYEZWA, H., STEWART, A., MALEKA, D. & MUSENGE, E. 2009. The International Classification of Function Disability and Health (ICF) in adults visiting the HIV outpatient clinic at a regional hospital in Johannesburg, South Africa. *AIDS care,* 21**,** 50-58.

VENTAFRIDDA, V. 2006. According to the 2002 WHO Definition of Palliative Care. *Palliative Medicine,* 20**,** 159.

VENTAFRIDDA, V., TAMBURINI, M., CARACENI, A., DE CONNO, F. & NALDI, F. 1987. A validation study of the WHO method for cancer pain relief. *Cancer,* 59**,** 850-856.

VICTOR, E. 2009. *A systematic review of interventions for carers in the UK: outcomes and explanatory evidence*, Princess Royal Trust for Carers.

VISSER, A., DECCACHE, A. & BENSING, J. 2001. Patient education in Europe: united differences. *Patient education and counseling,* 44**,** 1-5.

VOGL, D., ROSENFELD, B., BREITBART, W., THALER, H., PASSIK, S., MCDONALD, M. & PORTENOY, R. K. 1999. Symptom Prevalence, Characteristics, and Distress in AIDS Outpatients. *Journal of Pain and Symptom Management,* 18**,** 253-262.

WADLEY, A., CHERRY, C., PRICE, P. & KAMERMAN, P. 2010. *Pain associated with HIV-associated sensory neuropathy in a black South African cohort*, European Journal of Pain Supplements. Conference: 3rd International Congress on Neuropathic Pain Athens Greece. Conference Start: 20100527 Conference End: 20100530. Conference Publication: (var.pagings). 4 (1) (pp 90), 2010. Date of Publication: April 2010.

WADLEY, A. L., CHERRY, C. L., PRICE, P. & KAMERMAN, P. R. 2011. HIV Neuropathy Risk Factors and Symptom Characterization in Stavudine-Exposed South Africans. *Journal of Pain & Symptom Management,* 41**,** 700-706.

WAHAB, K. W. & SALAMI, A. K. 2011. Pain as a symptom in patients living with HIV/AIDS seen at the outpatient clinic of a Nigerian tertiary hospital. *Journal of the International Association of Physicians in AIDS Care (JIAPAC),* 10**,** 35-39.

WAKEHAM, K., HARDING, R., BAMUKAMA-NAMAKOOLA, D., LEVIN, J., KISSA, J., PARKES-RATANSHI, R., MUZAAYA, G., GROSSKURTH, H. & LALLOO, D. 2010. Symptom burden in HIV-infected adults at time of HIV diagnosis in rural Uganda. *J Palliat Med,* 13**,** 375 - 380.

WAKEHAM, K., HARDING, R., PARKES, R., BAMUKAMA, D., LEVIN, J., MUZAAYA, G., KAMALI, A. & LALLOO, D. 2009. *The symptom prevalence and burden in HIV-1-infected adults in rural Uganda*, HIV Medicine. Conference: 15th Annual Conference of the British HIV Association Liverpool United Kingdom. Conference Start: 20090401 Conference End: 20090403. Conference Publication: (var.pagings). 10 (pp 43), 2009. Date of Publication: April 2009.

WALKER, D., BARNETT, P., BURTON, S., MEECHAM, E. & THOMPSON, B. 2012. What is Arthritis? : Arthritis Research UK.

WALSH, K., JONES, L., TOOKMAN, A., MASON, C., MCLOUGHLIN, J., BLIZARD, R. & KING, M. 2007. Reducing emotional distress in people caring for patients receiving specialist palliative care. *British Journal of Psychiatry,* 190**,** 142 - 147.

WALSH, T. M. & VOLSKO, T. A. 2008. Readability Assessment of Internet-Based Consumer Health Information. *Respiratory Care,* 53**,** 1310-1315.

WANG, H., ZHOU, J., HUANG, L., LI, X., FENNIE, K. P. & WILLIAMS, A. B. 2010. Effects of nurse-delivered home visits combined with telephone calls on medication adherence and quality of life in HIV-infected heroin users in Hunan of China. *Journal of clinical nursing,* 19**,** 380-388.

WANTLAND, D. J., HOLZEMER, W. L., MOEZZI, S., WILLARD, S. S., ARUDO, J., KIRKSEY, K. M., PORTILLO, C. J., CORLESS, I. B., ROSA, M. E., ROBINSON, L. L., NICHOLAS, P. K., HAMILTON, M. J., SEFCIK, E. F., HUMAN, S., RIVERO, M. M., MARYLAND, M. & HUANG, E. 2008a. A Randomized Controlled Trial Testing the Efficacy of an HIV/AIDS Symptom Management Manual. *Journal of Pain and Symptom Management,* 36**,** 235-246.

WARD, S., DONOVAN, H., GUNNARSDOTTIR, S., SERLIN, R. C., SHAPIRO, G. R. & HUGHES, S. 2008. A randomized trial of a representational intervention to decrease cancer pain (RIDcancerPain). *Health Psychology,* 27**,** 59.

WARD, S., DONOVAN, H. S., OWEN, B., GROSEN, E. & SERLIN, R. 2000. An individualized intervention to overcome patient-related barriers to pain management in women with gynecologic cancers. *Research in nursing & health,* 23**,** 393-405.

WARD, S. E., SERLIN, R. C., DONOVAN, H. S., AMERINGER, S. W., HUGHES, S., PE-ROMASHKO, K. & WANG, K.-K. 2009. A randomized trial of a representational intervention for cancer pain: does targeting the dyad make a difference? *Health Psychology,* 28**,** 588.

WATSON, M., LUCAS, C., HOY, A. & WELLS, J. 2009. *Oxford handbook of palliative care,* Oxford, Oxford University Press.

WEBB, C. & ROE, B. 2007. *Reviewing research evidence for nursing practice.,* Oxford, Blackwell Publishing.

WEBEL, A. R. 2010. Testing a peer-based symptom management intervention for women living with HIV/AIDS. *AIDS care,* 22**,** 1029-1040.

WELLS, N., HEPWORTH, J. T., MURPHY, B. A., WUJCIK, D. & JOHNSON, R. 2003. Improving Cancer Pain Management Through Patient and Family Education. *Journal of Pain and Symptom Management,* 25**,** 344-356.

WENTZ, J. D. 2005. Managing pain in a patient with HIV or AIDS. *Nursing,* 35**,** 28-28.

WHITE, I. R., HORTON, N. J., CARPENTER, J., MEDICAL, R. I., STATISTICS, S. & POCOCK, S. J. 2011. Strategy for intention to treat analysis in randomised trials with missing outcome data. *BMJ,* 342.

WHO 1990. Cancer pain relief and palliative care: report of a WHO expert committee *WHO tech rep ser,* 804**,** 1-75.

WHO 1996. Cancer pain relief with a guide to opioid availability. *In:* WHO (ed.) Second Edition ed. Geneva.

WHO. 1998. WHO definition of palliative care. Available: http://www.who.int/cancer/palliative/definition/en/.

WHO 2002. National cancer control programmes: policies and managerial guidelines. *In:* WHO (ed.). Geneva.

WHO 2005. Interim WHO clinical staging of HIV/AIDS and HIV/AIDS case definitions for Surveillance: Treat 3 million by 2005. *In:* WHO (ed.). Geneva.

WHO. 2006a. The Impact of AIDS on people and societies. *2006 Report on the Global AIDS Epidermic* [Online]. Available: http://www.who.int/hiv/mediacentre/2006_GR_CH04_en.pdf?ua=1 [Accessed 10/04/2014].

WHO 2006b. The urgency of pain control in adults with HIV/AIDS: HIV/AIDS cancer pain release.

WHO. 2007. *WHO case definitions of HIV for surveillance and revised clinical staging and immunological classification of HIV-related disease in adults and children.* [Online]. Available: http://www.who.int/hiv/pub/guidelines/HIVstaging150307.pdf [Accessed Accessed: 24/11/11.

WHO 2010. Antiretroviral therapy for HIV infection in Adults and Adolescents: Recommendations for a public health approach. *In:* PROGRAMME, H. A. (ed.). Geneva.

WHO 2011a. Cooperation strategy at a glance.

WHO 2011b. Global HIV/AIDS Response – Epidemic update and health sector progress towards Universal Access – Progress Report 2011. *In:* WHO (ed.). Geneva.

WHO 2013. HIV Treatment Global Update on HIV Treatment 2013: Results, Impact and Opportunities

WHO/UNAIDS/UNICEF 2011. Global HIV/AIDS Response: Epidemic update and health sector progress towards Universal Access

WU, A. W., SNYDER, C. F., HUANG, I., SKOLASKY, R., JR., MCGRUDER, H. F., CELANO, S. A., SELNES, O. A. & ANDRADE, A. S. 2006. A randomized trial of the impact of a programmable medication reminder device on quality of life in patients with AIDS. *AIDS Patient Care & Stds,* 20**,** 773-781.

YATES, P., EDWARDS, H., NASH, R., ARANDA, S., PURDIE, D., NAJMAN, J., SKERMAN, H. & WALSH, A. 2004. A randomized controlled trial of a nurse-administered educational intervention for improving cancer pain management in ambulatory settings. *Patient Education and Counseling,* 53**,** 227-237.

YEGUEZ, J. F., MARTINEZ, S. A. & SANDS, D. R. 2003. Colorectal malignancies in HIV-positive patients *Am Surg,* 69**,** 981-7.

YILDIRIM, Y. K., CICEK, F. & UYAR, M. 2009. Effects of Pain Education Program on Pain Intensity, Pain Treatment Satisfaction, and Barriers in Turkish Cancer Patients. *Pain Management Nursing,* 10**,** 220-228.

ZECH, D. F. J., GROND, S., LYNCH, J., HERTEL, D. & LEHMANN, K. A. 1995. Validation of World Health Organization Guidelines for cancer pain relief: a 10-year prospective study. *Pain,* 63**,** 65-76.

ZOLLER, K. & HARRISON, B. 2007. Adult learning theories and practices. *The Advanced Facilitation Skills Course* [Online]. Available: http://sph.bu.edu/otlt/teachingLibrary/Learning%20Theory/adultlearning.pdf [Accessed 23/10/2013].

ZUBIETA, J.-K., SMITH, Y. R., BUELLER, J. A., XU, Y., KILBOURN, M. R., JEWETT, D. M., MEYER, C. R., KOEPPE, R. A. & STOHLER, C. S. 2002. μ-Opioid receptor-mediated antinociceptive responses differ in men and women. *The Journal of neuroscience,* 22**,** 5100-5107.

APPENDICES

Appendix 1: Participants Information Sheet (for patients and carers)

University of Nottingham
School of Nursing, Midwifery and Physiotherapy
Division of Nursing

Title of project: Managing pain in HIV/AIDS: education for people living with HIV/AIDS and their family carers

Researchers: Kennedy Nkhoma, Prof. Antony Arthur, Prof. Jane Seymour

Participant Information Sheet (People living with HIV/AIDS)

We would like to invite you to take part in a research study. Before you decide whether to take part it is important that you read the information contained below. We encourage you to discuss this information with family members or friends. Please contact Kennedy Nkhoma (pain education nurse) or one of the clinic staff if there is any clarification you need or any information not contained within this document. Please take your time to decide whether you wish to take part or not in the study.

Background and purpose of the study?

The study aims to investigate the effects of an educational intervention on the experience of pain and managing pain among people living with HIV/AIDS. We know that pain is frequently experienced and difficult to manage in HIV infection; we therefore want to assess if providing people living with HIV/AIDS and their family carers with a short educational package will help the way pain is managed. It is hoped that this in turn will assist in reducing the pain experienced. The study will take two months to complete.

What does the study involve?

If you agree to take part we will ask you to sign a consent form. Thereafter Kennedy Nkhoma (pain education nurse) will conduct a short series of baseline assessments through the administration of a questionnaire about your experiences and knowledge of pain. Together with the person who is your main carer, you will then be allocated into one of two groups. This allocation is determined by a computer (which has no information about participants). This means that you will have a 50% chance of being allocated to one particular group. In one group participants will receive health education via a face-to-face meeting with Kennedy Nkhoma and you will be given a leaflet about pain assessment and management. The other group will receive usual care. After eight weeks, when you come to the HIV clinic (accompanied by your main carer) for your routine appointment for HIV medication, a staff nurse will conduct follow-up assessments to study participants using the same interviewer administered questionnaire used for baseline assessments. If you

are allocated to usual care you will still receive the educational package about pain, but not until after you have completed the follow-up assessments.

Why have I been chosen?

You have been invited to take part in the research study because you are living with HIV/AIDS and you are in pain or at risk of experiencing pain. We require 179 volunteers like yourself to complete the study.

Do I have to take part?

It is entirely up to you whether you decide to take part or not. This information is given to you to think about in making that decision. You will have access to all services at the hospital that you would if you were not taking part in the study and regardless of which group you are allocated to. You are free to withdraw from the study at any time, you do not need to give a reason should you decide to withdraw, and your treatment will not be affected.

What do I have to do?

We ask that you take part in the interviewer-administered questionnaire at the beginning and end of the study. If you are allocated to the group that initially receive the educational package relating to pain, we ask that you do not discuss the contents of the leaflet with other patients or carers who may also be in the study. There is no need to alter your lifestyle during the duration of your involvement in the study.

What are the benefits of taking part in the study?

There are no direct benefits in taking part in the study. However this may be an opportunity for you to learn ways of assessing the pain you experience and how to better manage that pain.

What are the risks of taking part in the study?

There are no risks involved if you take part in the study and every effort will be made not to inconvenience you or your carer.

Where will the research take place?

The research has been designed to limit any inconvenience. The questionnaire you will complete at the beginning and end of the study will be administered at routine clinic appointments eight weeks apart. When you receive the educational package relating to pain management, this will be delivered at a place convenient to you and your carer (either at the hospital or in your own home depending on your choice).

What if something goes wrong?

If you have any concerns about your participation in the study, contact Kennedy Nkhoma, Ekwendeni College of Health Sciences, P.O. Box 49, Ekwendeni, phone number: 265991696828. Any issues not appropriately addressed by the researcher should be addressed to Dr C. Mwansambo of the National Health Sciences Research Committee, P.O. Box 30377, Lilongwe 3, Malawi.

Will my taking part in the study be kept confidential?

Data will be managed confidentially and securely by the researcher and will not be disclosed to anyone at the hospital or elsewhere. You will be given a unique number which means it will not be possible for researchers conducting the analysis to know the name of the participant. All information collected will be kept in a password protected database and will be strictly confidential.

What will happen to the results of the research study?

The results of the research study will help to develop educational interventions in assessing and managing pain among people living with HIV/AIDS. The results will be published in journal articles and conferences and will be written as a doctoral thesis. The results will also be shared with Ekwendeni hospital and other hospitals in the country which provide home-based care and palliative care services. No names and addresses or any personal identifying details will be used for publishing the results.

Who is funding the study?

The University of Nottingham School of Nursing, Midwifery and Physiotherapy and the Malawi Government. The study is being undertaken as a partial fulfillment for an educational qualification (PhD).

Who has reviewed this study?

The study has been reviewed by the University of Nottingham Medical School Ethics Committee and the National Health Sciences Research Committee in Malawi.

What if I want to take part?

It is very important that you discuss with your family or relevant others about taking part in the study. If you decide to take part in the study, please let any member of clinic staff know. Your details will be forwarded to Kennedy Nkhoma who will contact you at your next appointment. If you are still happy to take part you will be asked to complete a consent form.

Thank you for reading this information sheet

University of Nottingham
School of Nursing, Midwifery and Physiotherapy
Division of Nursing
Title of project: Managing pain in HIV/AIDS:

education for people living with HIV/AIDS and their family carers

Researchers: Kennedy Nkhoma, Prof. Antony Arthur, Prof. Jane Seymour

Participant Information Sheet (family carers)

We would like to invite you to take part in a research study. Before you decide whether to take part it is important that you read the information contained below. We encourage you to discuss this information with family members or friends. Please contact Kennedy Nkhoma (pain education nurse) or one of the clinic staff if there is any clarification you need or any information not contained within this document. Please take your time to decide whether you wish to take part or not in the study.

Background and purpose of the study?

The study aims to investigate the effects of an educational intervention on the experience of pain and managing pain among people living with HIV/AIDS. We know that pain is frequently experienced and difficult to manage in HIV infection; we therefore want to assess if providing people living with HIV/AIDS and their family carers with a short educational package will help the way pain is managed. It is hoped that this in turn will assist in reducing the pain experienced. The study will take two months to complete.

What does the study involve?

If you agree to take part we will ask you to sign a consent form. Thereafter Kennedy Nkhoma (pain education nurse) will conduct a short series of baseline assessments through the administration of a questionnaire about your experiences and knowledge of caring for someone who has pain. Together with the person who you care for, you will then be allocated into one of two groups. This allocation is determined by a computer (which has no information about participants). This means that you will have a 50% chance of being allocated to one particular group. In one group participants will receive health education via a face-to-face meeting with Kennedy Nkhoma and you will be given a leaflet about pain assessment and management. The other group will receive usual care. After eight weeks, when you come to the HIV clinic (accompanied by the person you care for) for your routine appointment for HIV medication, a staff nurse will conduct follow-up assessments to study participants using the same interviewer administered questionnaire used for baseline assessments. If

you are allocated to usual care you will still receive the educational package about pain, but not until after you have completed the follow-up assessments.

Why have I been chosen?

You have been invited to take part in the research study because you are a family carer of a person living with HIV/AIDS who is in pain or at risk of experiencing pain. We require 179 carers like you to complete the study.

Do I have to take part?

It is entirely up to you whether you decide to take part or not. This information is given to you to think about in making that decision. Your patient will have access to all services at the hospital that you would if you were not taking part in the study and regardless of which group you are allocated to. You are free to withdraw from the study at any time, you do not need to give a reason should you decide to withdraw, and the treatment of your patient will not be affected.

What do I have to do?

We ask that you take part in the interviewer-administered questionnaire at the beginning and end of the study. If you are allocated to the group that initially receive the educational package relating to pain, we ask that you do not discuss the contents of the leaflet with other patients or family carers who may also be in the study. There is no need to alter your lifestyle during the duration of your involvement in the study.

What are the benefits of taking part in the study?

There are no direct benefits in taking part in the study. However this may be an opportunity for you to learn ways of assessing the pain the person you care for experiences and how to better manage that pain.

What are the risks of taking part in the study?

There are no risks involved if you take part in the study and every effort will be made not to inconvenience you or the person you care for.

Where will the research take place?

The research has been designed to limit any inconvenience. The questionnaire you will complete at the beginning and end of the study will be administered at routine clinic appointments eight weeks apart. When you receive the educational package relating to pain management, this will be delivered at a place convenient to you and the person you care for (either at the hospital or in your own home depending on your choice).

What if something goes wrong?

If you have any concerns about your participation in the study, contact Kennedy Nkhoma, Ekwendeni College of Health Sciences, P.O. Box 49, Ekwendeni, phone number: 265991696828. Any issues not appropriately addressed by the researcher should be addressed to Dr C. Mwansambo of the National Health Sciences Research Committee, P.O. Box 30377, Lilongwe 3, Malawi.

Will my taking part in the study be kept confidential?

Data will be managed confidentially and securely by the researcher and will not be disclosed to anyone at the hospital or elsewhere. You will be given a unique number which means it will not be possible for researchers conducting the analysis to know the name of the participant. All information collected will be kept in a password protected database and will be strictly confidential.

What will happen to the results of the research study?

The results of the research study will help to develop educational interventions in assessing and managing pain among people living with HIV/AIDS. The results will be published in journal articles and conferences and will be written as a doctoral thesis. The results will also be shared with Ekwendeni hospital and other hospitals in the country which provide home-based care and palliative care services. No names and addresses or any personal identifying details will be used for publishing the results.

Who is funding the study?

The University of Nottingham School of Nursing, Midwifery and Physiotherapy and the Malawi Government. The study is being undertaken as a partial fulfillment for an educational qualification (PhD).

Who has reviewed this study?

The study has been reviewed by the University of Nottingham Medical School Ethics Committee and the National Health Sciences Research Committee in Malawi.

What if I want to take part?

It is very important that you discuss with the person you care for and family members or relevant others about taking part in the study. If you decide to take part in the study, please let any member of clinic staff know. Your details will be forwarded to Kennedy Nkhoma who will contact you at your next appointment. If you are still happy to take part you will be asked to complete a consent form.

Thank you for reading this information sheet.

University of Nottingham
School of Nursing Midwifery and Physiotherapy
Division of Nursing

Malonje ghakukhwaksana na kafukufuku

Mutu wa kafukufuku: Masambiro ghakukhwasyana na umo tingamupwelelera mulwali uyo wakupulika ulwilwi chifukwa cha matenda gha EDZI

Bakupanga kafukufuku: Kennedy Nkhoma, Dr Tony Arthur, Professor Jane Seymour

Pakudanga pokelani moni. Talemba kalata uyu kukhumba kumumanyiksani kuti tikupanga kafukufuku wa masambiro yakukhwaksana na umo tingasamalira munthu uyo wana kachibungu ka EDZI ndipo wakupulika ulwilwi muthupi. Sono tati mumanye kuti ndimwe banangwa kutorapo gawo pa kafukufuku uyu ndipo mukwenela kudumbiksana na wavwili winu. Pala pali chilichose icho mukukhumba kufumba mukhale wakumasuka pakufumba ba Kennedy Nkhoma awo wakwendeksa kafukufuku uyu.

Kasi chakulata cha kafukufuku uyu ntchivichi?

Chakulata cha kafukufuku uyu ntchakuti tikukhumba kumanya pala masambiro kwa banthu awo wakulwala matenda gha EDZI kweniso bavwili bawo yangawovwila pakupwelera kweniso kusamalira balwali na kuchepeska ulwilwi muthupi. Tikumanya kuti banthu abo wana kachibungu ka EDZI kawirikawiri bakupulika kuphwanya na ulwilwi muthupi.

Kasi kafukufuku wake ngwakuti wuli?

Pala mwapanga chisankho kuti mutole nawo gawo pa kafukufuku uyu, mukwenela kusayina pa kalata. Ndipo Kennedy Nkhoma uyo wakupanga na kwendeksa kafukufuku uyu wamufumbeninge mafumbo yakukhwasyana na ivyo imwe mukumanyapo paza kuphwanya muthupi, kweniso matenda gha EDZI.

Kufuma apo muzamukhala magulu ghawiri, guru lakwamba lizamupokela masambiro kweniso ka buku kakukhwaksana na kusamalira mulwali uyo wakupulika ulwilwi. Gulu la chiwiri lizamusambila pala pajumpha miyezi yiwiri, ndipo wazamupokelaso ka buku nawoso, kweni pala pajumpha miyesi yiwiri iyi mafumbo yala mukafumbika pakwamba yala muzamufumbikaso kuti tione pala masambiro yagwila ntchito panji yayi. Ndipo mafumbo aya wazamukufumbani ndi dokotala waku Wanangwa clinic.

Ntchifukwa uli nasankhika?

Chifukwa ndimwe yumoza wa awo wakupulika ulwilwi chifukwa cha matenda gha EDZI, kweniso chifukwa ndimwe bavwili ba abo wakulwala matenda gha EDZI.

Kasi ntchakuzilwa kutolapo nawo gawo?

Vyose vili kwa imwe pala mukukhumba kutolapo nawo gawo. Mupange chisankho pamoza na wa vwili winu. Sono pala mwazomelezgana kuti mutolengepo gawo tikupemphaninge kuti musayine kalata kuti mwapanga chisankho kutorapo gawo pa kafukufuku ndipo pala mukukhumba kulekela pa nthowa kafukufuku uyu palije sugzo, palije kuchichizgana pakuti ni wanangwa winu.

Kasi phindu la kafukufuku uyu ni vichi?

Phindu lake pasono pano lingamanyikwa viwi yayi kwa imwe kweni panji chingawa chakuzilwa kwa imwe kuti musambile nthowa ziweme zakupwelelera mulwali pala wakupulika ulwilwi muthupi

Kasi ni masuzgo wuli agho ningasangana nagho pala natola gawo pa kafukufuku uyu?

Palije suzgo lililose ilo mungakumana nalo pala mwatolapo gawo pa kafukufuku uyu, kweni mukwenela kumanya kuti pazamukhumbika nyengo yakuti timufumbeni mafumbo kweniso kuti pazamukhumbika nyengo yakuti muzasambile ndipo pala mwasambila muzamupokela ka buku ka masambilo ako mwamuwazgila ku nyumba.

Kweniso awo wali mu gulu lachiwiri wakwenela kulindila miyezi iwiri kuti wazapokele masambiro kweniso ka buku ka masambilo.

Kasi kafukufuku wachitikilenge nkhuni?

Ku chipatala cha Ekwendeni ku Wanangwa clinic naku chipatala cha Mzuzu central ku Rainbow clinic

Sono pala pali suzgo kwakudandaula ninkhu?

Pala pali suzgo lililose panji fumbo lililose lakukhwaksana na kafukufuku uyu, yimbani phoni pa nambala iyi 0888715056 panji 0991696828, kuti muyowoye na Kennedy Nkhoma. Pala mundawovwilike yimbani ku likulu lakuona kafukufuku ku Lilongwe pa nambala iyi 0999218630 kuti muyowoye na a Mr Bob Majamanda.

Sono kasi chisisi chilipo?

Mazina ghose ghazamugwilisyika ntchito yayi, ndipo pakuthandazga kafukufuku uyu tizamugwiliksa ntchito mazina yayi.

Sono kasi ivyo mwasanga pa kafukufuku uyu muzamuchita navyo uli?

Vyose ivyo tizamusanga pa kafukufuku uyu, vizamuvwila kuti wanthu wose awo wana matenda gha EDZI wasambizgikenge ku chipatala umo wangasamalira balwali awo wakupulika ulwilwi ku nyumba.

Kasi mbanjani awo wakupanga kafukufuku uyu

Sukulu ya univesite yaku Engilande mwakovwilana na boma la Malawi, ndipo kafukufuku uyu wakulongozgeka na mwana wa sukulu ku Engilande.

Kasi kafukufuku uyu wamuzomelezga?

Inya bungwe lakuona za kafukufuku muno mu Malawi laku Ministry ya Health, kweniso bungwe lakuona za kafukufuku ku sukulu yaku Engilande wose wawunika nakuzomelezga kafukufuku uyu.

Kasi pala tapanga chisankho kuti titole nawo gawo tichite uli?

Pala mukukhumba kutolapo gawo chakudanga waphalileni wa vwili winu ndipo mukwenela kuzomelezgana. Pala mwapulikana wamanyikseni a Kennedy Nkhoma panji waliyose uyo mwamusanga ku Wanangwa clinic.

Tamuwongani chomene pakuwelenga kalata uyu.

Appendix 2 Consent forms (for patients and carers)

University of Nottingham
School of Nursing Midwifery and Physiotherapy
Division of Nursing

Title of project: Managing pain in HIV/AIDS: education for people living with HIV/AIDS and their family carers

Researchers: Kennedy Nkhoma, Prof. Antony Arthur, Prof. Jane Seymour

Consent form (for people living with HIV/AIDS)

Please read this form and sign it if you wish to participate in the study.

I voluntarily agree to participate in the study.	☐
I confirm that I have been given a full explanation by the researcher. I have read and understood the information sheet.	☐
I have had the opportunity to ask questions and discuss the aims of the study with the researcher and I have understood the information and advice given as a result.	☐
I agree to comply with the reasonable instructions of the supervising investigator and will notify him immediately of any unexpected unusual symptoms or deterioration of health.	☐
I agree to use the results from the study in published reports, and presentations.	☐
I understand that my personal details will not be included in the results and publication or any other output from the research.	☐
I understand that information about me recorded during the study will be kept in a secure database. If data is transferred to others it will be made anonymous. Data will be kept for 7 years after the results of this study have been published.	☐
I understand that I can ask for further clarification at any time.	☐
I understand that I can withdraw from the study at any given time without giving any reason.	☐
I confirm that I have disclosed relevant medical information before the study.	☐

Name**:** ……

Address: ……..

Telephone number: …….

Signature: ……. Date: ……

I confirm that I have fully explained the purpose of the study and what is involved to:

……

I have given the above named a copy of this form together with the information sheet.

Investigators Signature: …….. Date: ……

Investigators Name:……

Study Volunteer Number: ……..

University of Nottingham
Schoolof Nursing Midwifery and Physiotherapy
Division of Nursing

Chiphaso chakuzomelezga kuchita nawo kafukufuku

Mutu wa kafukufuku: Masambiro ghakukhwaksana na umo tingamupwelelera mulwali uyo wakupulika ulwilwi chifukwa cha matenda gha EDZI

Bakupanga kafukufuku: Kennedy Nkhoma, Profesa Tony Arthur, Profesa Jane Seymour

Chonde welengani ndipo masayinile pala mwazomela kutola nawo gawo pa kafukufuku

Ine napanga chisankho pandekha kutola nawo gawo pa kafukufuku.	☐
Nkhusimikizga kuti ndapokela uthenga wakwenelera na wakukwana wakukhwaksana na kafukufuku ndipo napulikiksa makola	☐
Nkhapika mwabi na mpata wakufumba mafumbo kwa awo wakupanga kafukufuku uyu chomene chomene kukhwaksana na chakulata cha kafukufuku.	☐
Nkhuzomela kulondezga malamgo gha kafukufuku uyu ndipo nkhusimikizga kuti ndizamuwaphalira awo wakwendeksa kafukufuku uyu pala kalikose kaheni kanisanga	☐
Nkhuzomela kuti ivyo kafukufuku uyu bazasanga wazalengezge kuti vizawovwile kusamalira walwali wanyakhe munthazi	☐
Ndine wakupulikiksa kuti wamugwiliksa ntchito zina lane yayi pakulengeza kafukufuku uyu	☐
Ndine wakupulikiksa kuti vyose vyakukhwaksana na kafukufuku uyu wamusungika mwa chisisi vyose ivyo tamudumbiksana	☐
Ndapulikiksa kuti ningafumba chilichose icho nindapulikikse kukhwaksana na kafukufuku uyu nyendo yili yose	☐
Ndine wakupulikiksa kuti ndingalekezga pa nthowa nyengo yili yose pala nakhumba	☐
Nkhuzomelezga kuti ndiyowoyenge matenda ghane kwa awo wakupanga kafukufuku	☐

Zina la mulwali:……..

Siginecha:…….. Dazi:…….

Address……..Phone number…….

Zina la wakupanga kafukufuku…….

Siginecha:…… Dazi:…….

University of Nottingham
School of Nursing Midwifery and Physiotherapy
Division of Nursing

Title of project: Managing pain in HIV/AIDS: education for people living with HIV/AIDS and their family carers

Researchers: Kennedy Nkhoma, Professor Antony Arthur, Prof. Jane Seymour

Consent form (for family carers)

Please read this form and sign it if you wish to participate in the study.

I voluntarily agree to participate in the study.	☐
I confirm that I have been given a full explanation by the researcher. I have read and understood the information sheet.	☐
I have had the opportunity to ask questions and discuss the aims of the study with the researcher and I have understood the information and advice given as a result.	☐
I agree to comply with the reasonable instructions of the supervising investigator and will notify him immediately of any unexpected unusual symptoms or deterioration of health.	☐
I agree to use the results from the study in published reports, and presentations.	☐
I understand that my personal details will not be included in the results and publication or any other output from the research.	☐
I understand that information about me recorded during the study will be kept in a secure database. If data is transferred to others it will be made anonymous. Data will be kept for 7 years after the results of this study have been published.	☐
I understand that I can ask for further clarification at any time.	☐
I understand that I can withdraw from the study at any given time without giving any reason.	☐

Name: ……

Address: ……..

Telephone number: …….

Signature: ……. Date: …….

I confirm that I have fully explained the purpose of the study and what is involved to:

……..

I have given the above named a copy of this form together with the information sheet.

Investigators Signature: …….. Date: ……

Investigators Name:……

Study Volunteer Number: ……..

University of Nottingham
School of Nursing Midwifery and Physiotherapy
Division of Nursing

Chiphaso chakuzomelezga kuchita nawo kafukufuku

Mutu wa kafukufuku: Masambiro ghakukhwaksana na umo tingamupwelelera mulwali uyo wakupulika ulwilwi chifukwa cha matenda gha EDZI

Bakupanga kafukufuku: Kennedy Nkhoma, Profesa Tony Arthur , Profesa

Jane Seymour

Chonde welengani ndipo masayinile pala mwazomela kutola nawo gawo pa kafukufuku.

Ine napanga chisankho pandekha kutola nawo gawo pa kafukufuku.	☐
Nkhusimikizga kuti ndapokela uthenga wakwenelera na wakukwana wakukhwaksana na kafukufuku ndipo napulikiksa makola	☐
Nkhapika mwabi na mpata wakufumba mafumbo kwa awo wakupanga kafukufuku uyu chomene chomene kukhwaksana na chakulata cha kafukufuku.	☐
Nkhuzomela kulondezga malamgo gha kafukufuku uyu ndipo nkhusimikizga kuti ndizamuwaphalira awo wakwendeksa kafukufuku uyu pala kalikose kaheni kanisanga	☐
Nkhuzomela kuti ivyo kafukufuku uyu bazasanga wazalengezge kuti vizawovwile kusamalira walwali wanyakhe munthazi	☐
Ndine wakupulikiksa kuti wamugwiliksa ntchito zina lane yayi pakulengeza kafukufuku uyu	☐
Ndine wakupulikiksa kuti vyose vyakukhwaksana na kafukufuku uyu wamusungika mwa chisisi vyose ivyo tamudumbiksana	☐
Ndapulikiksa kuti ningafumba chilichose icho nindapulikikse kukhwaksana na kafukufuku uyu nyendo yili yose	☐
Ndine wakupulikiksa kuti ndingalekezga pa nthowa nyengo yili yose pala nakhumba	☐

Zina la movwili:……

Siginecha:……..Dazi:……

Address:…… Phone number:……..

Zina la wakupanga kafukufuku:…….

Siginecha:…… Dazi:…….

Appendix 3: Check list for eligibility

Inclusion criteria for patients

Diagnosis of HIV/AIDS? ☐

Aged 18 years and above? ☐

Catchment area 20km radius? ☐

Stage III or IV HIV/AIDS or CD4 <350 ☐

Able to read English or Tumbuka? ☐

Inclusion criteria for family carers ☐

Primary family carer for the patient? ☐

Aged 18 years and above? ☐

Able to read English or Tumbuka? ☐

Do you stay/live with the patient? ☐

Appendix 4: Demographic data for study participants

Patient characteristics

Patient name ……

Date of birth/age……

Gender……

Religion……

Occupation……

Address……

Source of referral……

Date of referral……..

Date of initial approach……..

Current treatment……..

Clinical stage of HIV/AIDS……

Co-morbidity……

Carers' characteristics

Carers' name……

Date of birth/age……

Gender……

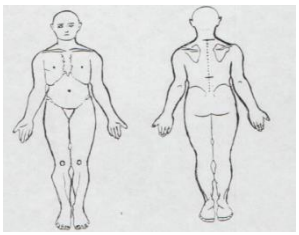
Religion……..

Occupation……..

Address……..

Carer's relationship with the patient……..

Appendix 5 Brief Pain Inventory



Date: ----------

Participant Number ----------

1. on the diagram, shade in the areas where you feel pain. Put an X on the area that hurts most.

1. Please rate your pain by circling the one number that best describes your pain at its **worst** in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

2. Please rate your pain by circling the one number that best describes your pain at its l**east** in the last week.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

3. Please rate your pain by circling the one number that best describes your pain on average.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

4. Please rate your pain by circling the one number that tells how much pain you have **right now**.

0 1 2 3 4 5 6 7 8 9 10

No pain Pain as bad as you can imagine

5. What treatments or medications are you receiving for your pain

_____

_____

7.In the last week, how much relief have pain treatments or medications provided? Please circle the one percentage that best shows how much relief you have received.

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

No relief Complete relief

8.Circle the one number that describes how, during the past week, pain has interfered with your:

a. General activity

0 1 2 3 4 5 6 7 8 9 10

Does not interfere Completely interferes

b. Mood

0 1 2 3 4 5 6 7 8 9 10

c. Walking ability

0 1 2 3 4 5 6 7 8 9 10

d. Normal work (includes both outside the home and housework)

0 1 2 3 4 5 6 7 8 9 10

e. Relations with other people

0 1 2 3 4 5 6 7 8 9 10

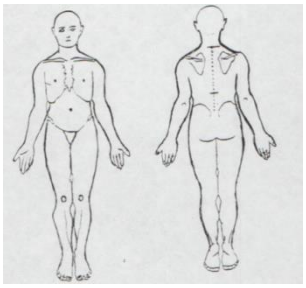
f. Sleep

0 1 2 3 4 5 6 7 8 9 10

g. Enjoyment of life

0 1 2 3 4 5 6 7 8 9 10

Does not interfere Completely interferes



Date: ----------

Participant Number ----------

1. Pa chipikichala ichi longolani ndipo lembani apo mukupulika ulwilwi.

2. Sankhani mulingo wa ulwilwi (**kuwinya chomone**) umo mwajipulikilanga sabata yamalanga iyi

0 1 2 3 4 5 6 7 8 9 10

No ulwilwi kuwinya chomene nkhanila

3. Sankhani mulingo wa ulwilwi **(kuwinya kachoko)** umo mwajipulikilanga sabata yamalanga iyi

0 1 2 3 4 5 6 7 8 9 10

No ulwilwi kuwinya chomene nkhanila

4. Sankhani mulingo wa ulwilwi **(kuwinya mwa pakatikati)** umo mwajipulikilanga mu sabata yamala iyi

0 1 2 3 4 5 6 7 8 9 10

No ulwilwi kuwinya chomene nkhanila

5. Sankhani mulingo wa ulwilwi umo mukujipulikila pasono pano

0 1 2 3 4 5 6 7 8 9 10

No ulwilwi kuwinya chomene nkhanila

6. Pasono pano mukupokela mankhwala wuli yakumazga ulwilwi?

_____

_____

7.Sankhani nambala iyo yikulongola mulingo wa ovwili uwo mankhawala yakupozga ulwilwi yagwilira ntchito muthupi mwinu

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

Yawovwila yayi Yawovwila chomene

8.Sankhani nambala iyo yikulongola umo ulwilwi muthupi wangumutimbanizgilani pa vinthu ivi mu sabata yamala iyi:

h. Ntchito zakupambana pambana

0 1 2 3 4 5 6 7 8 9 10

Zangutimbanizgikayayi zangutimbanizgika chomene

Maghanoghano mumutu?

0 1 2 3 4 5 6 7 8 9 10

Yayi chomene

i. Pakwenda

0 1 2 3 4 5 6 7 8 9 10

j. Mulimo yapanyumba

0 1 2 3 4 5 6 7 8 9 10

k. Kuchezga kweneso pa makhaliro na wanyane wose

0 1 2 3 4 5 6 7 8 9 10

l. Pa ugonero(kugona tulo)

0 1 2 3 4 5 6 7 8 9 10

m. Kukondwela na umoyo

0 1 2 3 4 5 6 7 8 9 10

Nangutimbanizgikayayi vangunitimbanizga chomene

Appendix 6 Patient Pain Questionnaire

Below are a number of statements about cancer pain/HIV/AIDS pain and pain relief. Please circle a number on the line to indicate your response.

Knowledge

1. HIV/AIDS/Cancer pain can be effectively relieved.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

2. Pain medicines should be given only when pain is severe.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

3. Most AIDS/cancer patients on pain medicines will become addicted to the medicines over time.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

4. It is important to give the lowest amount of medicine possible to save larger doses for later when the pain is worse.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

5. It is better to give pain medications around the clock (on a schedule) rather than only when needed.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

6. Treatments other than medications (such as massage, heat, relaxation) can be effective for relieving pain.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

7. Pain medicines can be dangerous and can often interfere with breathing.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

8. Patients are often given too much pain medicine.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

9. If pain is worse, the cancer/ AIDS must be getting worse.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

Experience

10. Over the past week, how much pain have you had?

No pain 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

11. How much pain are you having now?

No pain 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

12. How much pain relief are you currently receiving?

A great deal 0 1 2 3 4 5 6 7 8 9 10 **no relief**

13. How distressing is the pain to you?

Not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

14. How distressing is your pain to your family members?

Not at all 0 1 2 3 4 5 6 7 8 9 10 **extremely**

15. To what extent do you feel you are able to control your pain?

Extremely 0 1 2 3 4 5 6 7 8 9 10 **not at all**

16. What do you expect will happen with your pain in the future?

Pain will 0 1 2 3 4 5 6 7 8 9 10 **pain will**

get better **get worse**

Sono apa tiwonenge vinji mwa vinthu ivyo wanthu wakuyowoya vyakukhwaksana na matenda gha kachibungu ka EDZI.

Ivyo mukumanyapo (Knowledge)

1 Ulwilwi wa matenda gha EDZI/kansa ungapozgeka.

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

2 Mankhwala yakupozga ulwilwi yapelekeke kwa mulwali pala ulwilwi wakwela chomene.

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

3 Walwali awo wakupokera mankhwala yakupozga ilwilwi kanandi kanandi wangakhala yayi kwambula mankhwala chifukwa wakuzgowela kukhalira mankhwala pela

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

4 Mankwala yakupozga ulwilwi timupenge mulwali pala ulwilwi wakwela chomene

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

5 Ntchiwemi kupereka mankhwala kulingana na nyengo kulekana na kulindira kuti ulwilwi uyambe

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

6 Nthowa zinyakhe nthena kukhanda na kasalu ka maji, kunyolora malundi, kuchita ma ekisasaizi vikovwila kupozga ulwilwi

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

7 Mankhwala yakupozga ulwilwi yakupangiksa kuti mulwali pala wamwa watondeke kuthutha makola

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

8 Kanandi kanandi walwali wakupokela mankwala yanandi chomene yakupozga ulwirwi

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

Umo mwajipulikilanga

9 Pala ulwilwi wakwela chomene nikuti EDZI nayo yafala chomene

Nkhusuksa 0 1 23 4 5 6 7 8 9 10 **Nkhuzomelezga**

10 Musabata yamala iyi mwapulika ulwilwi wuli? Sankhani nambala yimoza apa

No ulwilwi 0 1 2 3 4 5 6 7 8 9 10 **Ulwilwi chomene**

11 Pasono pano mukupulika mulingo wuli wa ulwilwi, sankhani nambala yimoza apa?

No ulwilwi 0 1 2 3 4 5 6 7 8 9 10 **Ulwilwi chomene**

12 Kasi mankhwala yakupozga ulwilwi yakumuwovwilani?

Yakovwilachomene 0 1 2 3 4 5 6 7 8 9 10 **yayi**

13 Kasi ulwilwi ukumupani maghanoghano imwe?

Yayi 0 1 2 3 4 5 6 7 8 9 10 **chomene**

14 Kasi ulwilwi ukuwapa maghanoghano wabale winu na wavwili winu?

Yayi 0 1 2 3 4 5 6 7 8 9 10 **chomene**

15 Kasi pa imwe mwekha mukukwaniksa kujiwovwila kuti ilwilwi upole muthupi mwinu?

Nkhukwaniksa 0 1 2 3 4 5 6 7 9 10 **Nkhukwaniksa yayi**

16 Kasi munthazi ulwilwi winu upolenge umo mukuwonela imwe?

Inya upolenge 0 1 2 3 4 5 6 7 8 9 10 **Yayinthe**

Appendix 7: APCA African POS

ASK THE PATIENT	
Q1.Please rate your pain (from 0 = no pain to 5 = worst/overwhelming pain) during the last 3 days	0 (no pain) - 5 (worst/overwhelming pain)
Q2. Have any other symptoms (e.g. nausea, coughing or constipation) been affecting how you feel in the last 3 days?	0 (not at all) - 5 (overwhelmingly)
Q.3 Have you been feeling worried about your illness in the past 3 days?	0 (not at all) - 5 (overwhelming worry)
Q.4 Over the past 3 days, have you been able to share how you are feeling with your family or friends?	0 (not at all) - 5 (yes, I've talked freely)
Q5. Over the past 3 days have you felt that life was worthwhile?	0 (no, not at all) - 5 (Yes, all the time)
Q6. Over the past 3 days, have you felt at peace?	0 (no, not at all) - 5 (Yes, all the time)
Q7. Have you had enough help and advice for your family to plan for the future?	0 (not at all) - 5 (as much as wanted)
ASK THE FAMILY CARER	
Q.8 How much information have you and your family been given?	0 (none) - 5 (as much as wanted) N/A
Q9. How confident does the family feel caring for ____?	0 (not at all) - 5 (very confident) N/A
Q.10 Has the family been feeling worried about the Client over the last 3 days?	0 (not at all) - 5 (severe worry) N/A

African palliative care scale

Q1 Yowoyani mulingo wa **ulwilwi** (0 = no ulwilwi to 5 = kuwinya chomene) pa madazi yatatu yaluta agha?

[ ] 0 No ulwilwi

[ ] 1 Pachoko waka mwakuti nkhughanaghanako yayi

[ ] 2 Ulwilwi wapachoko mwakuti nkhutondeka tumilimo tunyakhe

[ ] 3 Ulwilwi ukuluko mwakuti nkhutondeka milimo

[ ] 4 Ulwilwi ukulu mwakuti nkhutondeka milimo kweneso kuteghelezga nkhutondeka

[ ] 5 Ulwilwi ukulu chomene nkhanila, nkhutondeka kuchita chilichose

Q2 Kasi mwanguwapo na masuzgo ghalighose nthena agha (**muselu, kubokola, chikhose**) mumadazi yatatu yaluta agha?

0 Yayi

1 Pachoko waka,

2 Mwapakatikati,

3 Chomene,

4 Chomene mwakujumphizga,

5 chomene mwakuti natondekanga kuchita mulimo

Q3. Kasi mwanguwa na **maghanoghano/kukhumudwa** na matenda ghinu pa madazi tatatu yaluta agha?

[ ] 0 Yayi

[ ] 1 Panyengopanyengo

[ ] 2 Panyengopanyengo mwakuti nkhutondeka kuti nichite milimo makola

[ ] 3 Nyengo yili yose maghanoghano mwapakati kati

[ ] 4 nyengo yilo yose maghanoghano yanandiko

[ ] 5 maghanoghano yakulu nadi, nyengo yili yose

Q4**.** Kasi mwawaphalirapo umo mukujipulikila na maghanoghano wanyinu/wanwezi kweneso wachibale winu?

[ ] 0 Yayi

[ ] 1 Pachoko waka

[ ] 2 Enya pakuti wakanifumba

[ ] 3 Enya kwene wangupulikiksa yayi

[ ] 4 Enya ndipo wangupulikiksa chomene

[ ] 5 Enya nanguwaphalira mwakumasuka chomene, ndipo wangupulikiksa

Q5. Pa madizi yatatu yaluta agha mwangujipulika kuti umoyo nguwemi, panji mwangujipulika makola?

[ ] 0 Yayi nthe

[ ] 1 Pa choko waka

[ ] 2 Munyengo-munyengo

[ ] 3 Nyengo zinyakhe enya

[ ] 4 Enya nyengo zose

[ ] 5 Enya nyengo zose, chomene nkhanila

Q6**.** Kasi pa madazi yatatu yaluta aya mwangukhala mwa mtende?

[ ] 0 Yayi

[ ] 1 panyengo panyengo/patali patali

[ ] 2 Nyengo zinyakhe enya

[ ] 3 Enya mwakukwanira

[ ] 4 Enya yengo zinandi

[ ] 5 Enya chomene, nyengo zose

Q7. Kasi mwapokela wovwili na malangizo na banja linu za umo mungakhalira umoyo wa munthazi?

[ ] 0 Yayi

[ ] 1 panyengo, panyengo/ mwapatali patali

[ ] 2 Enya nyengo zinyakhe

[ ] 3 Enya mwakukwanira

[ ] 4 Enya, nyengo zinandi

[ ] 5 Enya chomene umo nkhukhumbila

Q8. Kasi mwapokelapo visambizgo vyakukwana imwe na walwali winu?

[ ] 0 Yayi

[ ] 1 Enya, panyengo panyengo,

[ ] 2 Enya nyengo zinyakhe,

[ ] 3 Enya kwene mwakukhanila yayi,

[ ] 4 Enya mwakukwanila

[ ] 5 Enya chomene mwakukwanila umo nkhukhumbila

Q9**.** Kasi ndimwe wakulimba mtima ndiposo wakukhwima kupwelera mulwali winu?

[ ] 0 Yayi

[ ] 1 pachoko weka

[ ] 2 enya nyengo zinyakhe kwene mwakukayikila chomene ,

[ ] 3 Enya kwene mwakukayikila pachoko,

[ ] 4 Enya,

[ ] 5 Enya chomene

Q10. Kasi mwanguwapo na maghanoghano chifukwa cha matenda gha mulwali winu pa madazi ghatatu ghaluta agha?

[ ] 0 Yayi,

[ ] 1 panyengo, panyengo,

[ ] 2 Enya nyengo zinyakha-

[ ] 3 Enya, nyengo zose,

[ ] 4 Enya, chomene

[ ] 5 Enya chomene nkhanila, nkhukhalira waka maghonghano

Appendix 8 Family Pain Questionnaire

Below are a number of statements about HIV/AIDS/cancer pain and pain relief. Please circle a number on the line to indicate your response.

Knowledge

1. Cancer pain can be effectively relieved.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

2. Pain medicines should be given only when pain is severe.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

3. Most cancer patients on pain medicines will become addicted to the medicines over time.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

4. It is important to give the lowest amount of medicine possible to save larger doses for later when the pain is worse.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

5. It is better to give pain medications around the clock (on a schedule) rather than only when needed.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

6. Treatments other than medications (such as massage, heat, relaxation) can be effective for relieving pain.

Agree 0 1 2 3 4 5 6 7 8 9 10 **disagree**

7. Pain medicines can be dangerous and can often interfere with breathing.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

8. Patients are often given too much pain medicine.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

9. If pain is worse, the cancer must be getting worse.

Disagree 0 1 2 3 4 5 6 7 8 9 10 **agree**

Experience

10. Over the past week, how much pain do you feel your family member has had?

No pain 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

11. How much pain is your family member having now?

No pain 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

12. How much pain relief is your family member currently receiving?

a great deal 0 1 2 3 4 5 6 7 8 9 10 **no relief**

13. How distressing do you think the pain is to your family member?

Not at all 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

14. How distressing is your family members' pain to you?

Not at all 0 1 2 3 4 5 6 7 8 9 10 **a great deal**

15. To what extent do you feel you are able to control the patient's pain?

a great deal 0 1 2 3 4 5 6 7 8 9 10 **not at all**

16. What do you expect will happen with your family member's pain in the future?

will get better 0 1 2 3 4 5 6 7 8 9 10 **will get worse**

Mafumbo kwa wabale wa mulwali panji wovwili wa mulwali

Ivyo mukumanyapo pa matenda gha EDZI (Knowledge)

1 Ulwilwi wa matenda gha kansa/EDZI ungapozgeka.

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

2 Mankhwala yakupozga ulwilwi yapelekeke kwa mulwali pala ulwilwi wakwela chomene.

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

3 Walwali awo wakupokela mankhwala wakupozga ilwilwi kanandi kanandi wangakhala yayi kwambula kumwa mankhwala chifukwa wakuzgowela kukhalira mankhwala pela

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

4 Ntchiwemi kusunga mankwala ndipo kuti timupe mulwali pala ulwilwi wakwela chomene

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

Ntchiwemi kupereka mankhwala kulingana na nyengo kulekana na kupereka pala ulwilwi wayamba

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

5 Ntchowa zinyakhe nthena kukhanda na kasalu ka maji, kunyolora malundi, kuchita ma ekisasaizi vikovwila kupozga ulwilwi

Nkhuzomelezga 0 1 2 3 4 5 6 7 8 9 10 **Nkhusuksa**

6 Mankhwala yakupozga ulwilwi yakupangiksa kuti mulwali pala wamwa watondeke kuthutha makola

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

7 Kanandi kanandi walwali wakupokela mankwala yanandi chomene yakupozga ulwirwi

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

8 Pala ulwilwi wakwela chomene nikuti EDZI nayo yafala chomene muthipi

Nkhusuksa 0 1 2 3 4 5 6 7 8 9 10 **Nkhuzomelezga**

Ivyo mwaviwona pa mulwali winu (Experience)

10 Musabata yamalanga iyi, kasi mulwali winu wangupulika ulwilwi wa mulingo wuli?

No ulwilwi 0 1 2 3 4 5 6 7 8 9 10 **Ulwilwi chomene**

11 Pasono pano mulwali winu wana ulwilwi wa mulingo wuli?

No ulwilwi 0 1 2 3 4 5 6 7 8 9 10 **Ulwilwichomene**

12 Kasi mankhwala yakupozga ulwilwi yakovwila uli?

Chomene 0 1 2 3 4 5 6 7 8 9 10 **yakovwilayayi**

13 Kasi ulwilwi ukumupasa maghanoghano mulwali winu?

Yayi 0 1 2 3 4 5 6 7 8 9 10 **chomene**

14 Kasi ulwilwi wa mulwali winu ukumupani maghanoghani imwe?

Yayi 0 1 2 3 4 5 6 7 8 9 10 **chomene**

15 Kasi pa imwe mwekha mukukwaniksa kupozga ulwilwi wa mulwali winu?

Chomene 0 1 2 3 4 5 6 7 8 9 10 **Yayinthe**

16 Kasi mukuwona kuti ulwilwi wa mulwali winu muthazi umu upolenge?

Ulwilwi upolenge 0 1 2 3 4 5 6 7 8 9 10 **ulutililenge**

Appendix 9 Picot caregiver Rewards Scale

Now I'd like to talk to you about some of the ways people feel about caring for another person. Please tell me how you feel now about caring for your [SPOUSE]. Choose only one answer for each statement from the following: A great deal [4], Quite a lot [3], Somewhat [2], A little [1], or Not at all [0].

		Great deal	Quite a lot	Some what	A little	Not at all
1.	I feel God will bless me.	4	3	2	1	0
2.	I feel better about myself.	4	3	2	1	0
3.	I feel I have become a stronger, tolerant, and/or patient person around persons with sickness or handicaps.	4	3	2	1	0
4.	I feel having others say that taking care of my spouse is the right thing to do is important	4	3	2	1	0
5.	I feel someone will take care of me when I need it.	4	3	2	1	0
6.	I feel receiving a smile, touch, or eye contact from my [**spouse**] is important.	4	3	2	1	0
7.	I feel I have a closer relationship with my [**spouse**].	4	3	2	1	0
8.	I feel I have become a better person by learning new information.	4	3	2	1	0
9.	I feel I have become a better person by learning new ways to care for my spouse.	4	3	2	1	0
10.	I feel that I have made many new friends.	4	3	2	1	0
11.	I feel more important.	4	3	2	1	0
12.	I feel I have the freedom to make decisions that matter.	4	3	2	1	0
13.	I feel that receiving praise and admiration for my efforts from doctors, nurses and social workers is important.	4	3	2	1	0
14.	I feel happier now that I did before I started caring for my [**spouse**].	4	3	2	1	0

15.	I feel that caring for my [**spouse**] has made our family grow and work closer together.	4	3	2	1	0
16.	I feel my family members now look up to me because of my efforts under difficult circumstances.	4	3	2	1	0

Sono apa pali mafumbo yakukhwaksana umo wanthu wanji wakujipulikira pala wakupwelelera mulwali. Chonde imwe namwe yowoyani umo mukujipulikira para mukupereka ovwiri ku murwali winu. Sankhanipo chimoza pakati pa Chomene nkhanila [4], Chomene [3], Chomeneko [2], Pachoko [1], Yayinthe [0].

		Chomene Nkhanila	Chomene	Chomeneko (mwanthena)	Pachoko	Yayi nthe
1.	Nkhujiwona kuti chiuta wanitumbikenge.	4	3	2	1	0
2.	Nkhujupulika wene nawene.	4	3	2	1	0
3.	Nkhujipulika kuti nina nkhongono, ndipo nkhuzizipizga, pala nkhutewetela wanthu walwali.	4	3	2	1	0
4.	Nkhuzomelezga umo wanyakhe wakuyowoyela kuti kupwelelera mulwali wane ntchinthu chiwemi na chakukhumbikila	4	3	2	1	0
5.	Nkhuwona ndipo nkhugomezga kuti nane walipo awo wazamuniwovwila na kunipwelelera pala nkhukhumba wovwiri.	4	3	2	1	0
6.	Nkhuwona kuti pala mulwali wane wakunisekelera, kunimwemwetera, kwenese kunibeka mwa chitemwa ntchinthu chiwemi na chakukhumbikila.	4	3	2	1	0
7.	Nkhuwona kuti ine na mulwali wane	4	3	2	1	0

	tikukoleranako na kupulikana chomene.					
8.	Nkhuwona kuti nasambilako vinthu vinyakhe ndipo sono ndine munthu wakusinthika.	4	3	2	1	0
9.	Nkhuwona kuti nasambila nthowa zinyakhe zakupwelelara mulwali wane.	4	3	2	1	0
10.	Nkhuwona kuti napanga wabwezi wanyakhe sono.	4	3	2	1	0
11.	Nkhuwona ndipo nkhujipulika kuti ndine wakukhumbikira chomene.	4	3	2	1	0
12.	Nkhuwona kuti nina mazaza na wanangwa wakupanga ivyo nkhukhumba kukhwaksana na kusamalira mulwali wane.	4	3	2	1	0
13.	Ntchakukhumbikira ndiposo ntchiwemi kuti wa dokotola nama nurse wanilumbenge ndiposo kunilimbikiksa pa ntchito iyo nkhuchita yakupwelera mulwali wane.	4	3	2	1	0
14.	Ndine wakukondwa chomene madazi ghano kulekana na kale apo nkhawa kuti nindambe yayi kupwelelera mulwali wane.	4	3	2	1	0
15.	Nkhuwona kuti kupwelerera mulwali	4	3	2	1	0

	wane kwapangiksa kuti banja lithu likule kweneso tikukhala makola na kupulikana makola na kutewetela mulimo limoza.					
16.	Nkhuwona kuti sono banja lane lose likunigomezga chomene chifukwa cha milimo iyo nkhuteweta chomene chomene nyengo za matenda.	4	3	2	1	0

Appendix 10 Ethical approval from Nottingham Medical School Ethics Committee

Direct line/e-mail
+44 (0) 115 8231063
Louise.Sabir@nottingham.ac.uk

The University of Nottingham
Faculty of Medicine and Health Sciences

Medical School Research Ethics Committee
Division of Therapeutics & Molecular Medicine
D Floor, South Block
Queen's Medical Centre
Nottingham
NG7 2UH

Tel: +44 (0) 115 8231063
Fax: +44 (0) 115 8231059

27th April 2012

Mr Kennedy Nkhoma
PhD Student
c/o Dr Anthony Arthur
Associate Professor
Room B58, Sue Ryder Care Centre
School of Nursing Midwifery & Physiotherapy
QMC Campus
Nottingham University Hospitals
NG7 2UH

Dear Mr Nkhoma

Ethics Reference No: SNMP11042012 PLWHA Kennedy
Study Title: An educational intervention to reduce pain and improve pain management for people living with HIV/AIDS and their family carers in Malawi: randomised controlled trial.
Student Lead Investigator: Mr Kennedy Nkhoma, PhD student, School of Nursing Midwifery & Physiotherapy.
Supervisor/Chief Investigator: Dr Anthony Arthur, Associate Professor, Professor Jane Seymour, Sue Ryder Care Professor, School of Nursing, Midwifery and Physiotherapy

Thank you for the above application dated 11th April 2012 and the following documents were received:

- Letter for ethics.docx 05 April 2012
- Application form.doc 05 April 2012
- Information Sheet for family carers.docx 11 April 2012
- Consent form for family carersdocx.docx 11 April 2012
- Carers administered questionnaire.docx 05 April 2012
- Pain Education Poster.pptx final.pdf 05 April 2012
- Protocol.docx 05 April 2012
- Consent form for PLWHA.docx 11 April 2012
- Information Sheet for PLWHA.docx 11 April 2012
- Questionnaire for PLWHA.docx 05 April 2012
- E-mail response to Ethics queries 18 April 2012
- Letter of support from Osborn N.I. Mwalwanda, Chief Clinical Officer, Cordinator, Wananangwa HIV/AIDs Clinic, Ekwendeni Hospital, Malawi dated 19th April 2012

These have been reviewed and are satisfactory and the study protocol is approved.

Approval is given on the understanding that the Conditions of Approval set out below are followed.

Ethics Committee approval is sought from the National Health Science Research Committee in Malawi. Please can you submit a copy of the approval letter when it is available.

Conditions of Approval

You must follow the protocol agreed and any changes to the protocol will require prior Ethics' Committee approval.

This study is approved for the period of active recruitment requested. The Committee also provides a further 5 year approval for any necessary work to be performed on the study which may arise in the process of publication and peer review.

You promptly inform the Chairman of the Research Ethics Committee of

(i) Deviations from or changes to the protocol which are made to eliminate immediate hazards to the research subjects.

(ii) Any changes that increase the risk to subjects and/or affect significantly the conduct of the research.

(iii) All adverse drug reactions that are both serious and unexpected.

(iv) New information that may affect adversely the safety of the subjects or the conduct of the study.

(v) The attached End of Project Progress Report is completed and returned when the study has finished.

Yours sincerely

Dr Clodagh Dugdale
Chair, Nottingham University Medical School Research Ethics Committee

Medical School Research Ethics Committee
Membership 2011/2012

Chair	Dr Clodagh Dugdale, University Teacher in Sports and Exercise Medicine, Division of Orthopaedic and Accident Surgery, School of Clinical Sciences.
School	**Representative**
Biomedical Sciences	Dr Vince Wilson, Reader and Basic Scientist. Dr Liz Simpson, Chief Experimental Officer.
Molecular Medical Sciences	Dr David Turner, Clinical Associate Professor in Microbiology.
Community Health Sciences	Dr Gill Doddy, Clinical Associate Professor & Reader in General Adult Psychiatry, Division of Psychiatry
Clinical Sciences	Dr Abdol Nateri, Lecturer, Pre-Clinical Cancer Studies Division of GI Surgery
Graduate Entry Medical School	Dr Caroline Chapman, Associate Professor, Breast Surgery.
Clinical Sciences Human Development	Professor Harish Vyas, Consultant & Special Professor in Paediatric Intensive Care Unit and Respiratory Medicine, Children's Respiratory Unit, E Floor, East Block, QMC Campus, Nottingham University Hospitals Trust.
Primary Care	Dr Richard Knox, General Practitioner/ Part-time Lecturer Division of Primary Care, QMC Campus
School of Nursing, Midwifery and Physiotherapy	Dr Jayne Brown, Senior Research Fellow University of Nottingham, Sue Ryder Care Centre
Lay (Out of Faculty)	Professor Nigel White, Professor of Public International Law, School of Law, University of Nottingham. Lydia Davies-Bright, PhD Student, School of Law. Dr Mary Stephenson, Research Fellow, SPMMRC, School of Physics and Astronomy.
Medical Students nominated by ISC	To be appointed, 3rd Year Medical Student
Postgraduate Student Member	Prema Nirgude PhD student, Division of Psychiatry Catrin Middleton, PhD student, Division of Breast Surgery
Administrator	Mrs Louise Sabir, Division of Therapeutics & MM, School of Clinical Sciences

Appendix 11 Ethical approval from National Health Sciences Research Ethics committee in Malawi

Telephone: + 265 789 400
Facsimile: + 265 789 431
e-mail doccentre@malawi.net
All Communications should be addressed to:
The Secretary for Health and Population

In reply please quote No. MED/4/36c

MINISTRY OF HEALTH
P.O. BOX 30377
LILONGWE 3
MALAWI

18th June, 2012

Kenedy Nkhoma
University of Nottingham

Dear Sir/Madam,

RE: Protocol # 1023: An educational intervention to reduce pain and improve the management of pain among people living with HIV/AIDS and their family carers in Malawi: a randomized controlled trial

Thank you for the above titled proposal that you submitted to the National Health Sciences Research Committee (NHSRC) for review. Please be advised that the NHSRC has **reviewed** and **approved** your application to conduct the above titled study.

- **APPROVAL NUMBER : NHSRC # 1023**
  The above details should be used on all correspondence, consent forms and documents as appropriate.
- **APPROVAL DATE : 18/6/2012**
- **EXPIRATION DATE** :This approval expires **on 18/06/2013**
  After this date, this project may only continue upon renewal. For purposes of renewal, a progress report on a standard form obtainable from the NHSRC secretariat should be submitted one month before the expiration date for continuing review.
- **SERIOUS ADVERSE EVENT REPORTING** :All serious problems having to do with subject safety must be reported to the National Health Sciences Research Committee within 10 working days using standard forms obtainable from the NHSRC Secretariat.
- **MODIFICATIONS**: Prior NHSRC approval using standard forms obtainable from the NHSRC Secretariat is required before implementing any changes in the Protocol (including changes in the consent documents). You may not use any other consent documents besides those approved by the NHSRC.
- **TERMINATION OF STUDY**: On termination of a study, a report has to be submitted to the NHSRC using standard forms obtainable from the NHSRC Secretariat.
- **QUESTIONS**: Please contact the NHSRC on Telephone No. (01) 724418, 0999218630 or by e-mail on moh@gmail.com
- **Other:**
  Please be reminded to send in copies of your final research results for our records as well as for the Health Research Database.

Kind regards from the NHSRC Secretariat.

.....

FOR CHAIRMAN, NATIONAL HEALTH SCIENCES RESEARCH COMMITTEE

Appendix 12 Ethical Approval from Mzuzu Central Hospital

Telephone: 01 320 916 /
878 Fax:
320223/320973/270
directormch@malawi.net

In reply please quote No..
The Hospital Director, Mzuzu
Central Hospital, Private Bag
209, Luwinga,
Mzuzu 2.
1" October, 2012

Kennedy Nkhoma
C/o Rev. HM Nkhoma
University of
Livingstonia P.O. Box
112
Mzuzu

Dear Sir,

REQUEST FOR PERMISSION TO CONDUCT A RESEARCH STUDY

Refer to your letter dated 28th September, 2012 in which you requested for permission to carry out a study at Mzuzu Central hospital on the topic ***"An educational intervention to reduce pain and improve pain management for people living with HIV/AIDS and their family carers in Malawi: a randomised controlled trial".*** I am pleased to inform you that permission has been granted following review of the letter and accompanied documents.

Wishing you a nice study.

Yours sincerely,

BK Nyirenda

Research Coordinator For: THE HOSPITAL DIRECTOR

Appendix 13 Information leaflet

'All about your pain'

Pain is one of the symptoms that are commonly experienced in HIV infection. HIV pain is experienced due to two main reasons:

1. Due to advanced HIV infection such as: headache, general body weakness, neck pain, chest pains, painful swallowing.

2. Due to side effect of HIV medication such as: abdominal pain, feeling of shooting, stabbing on your hands and feet's which sometimes makes you unable to walk or hold anything with your hands.

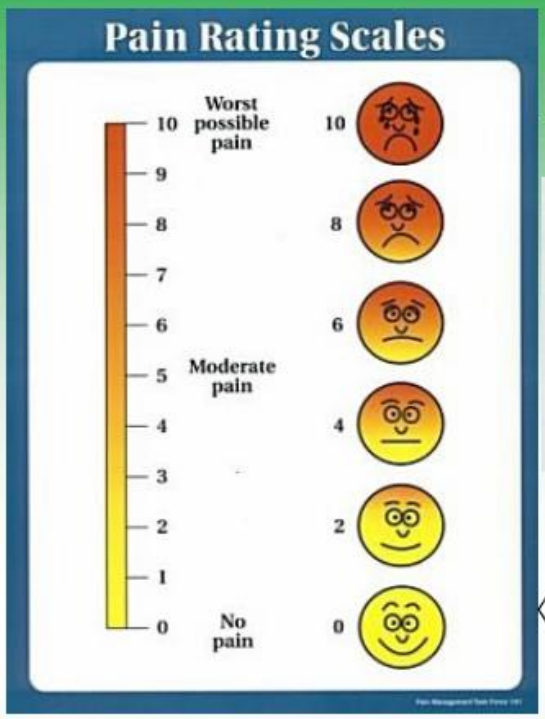
When you experience any form of pain , it is important to come to the hospital to be examined by the doctor.

Even though pain will always be experienced it can easily be managed even at home. This booklet will teach you how to assess pain and manage it at home.

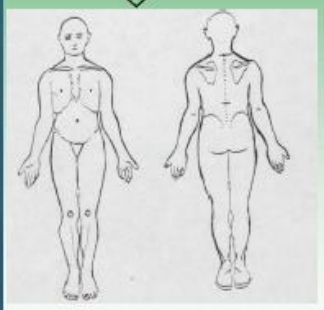
Pain Assessment

Using pain diagrams:

- You can locate your pain.
- Describe how you experience the pain like shooting, burning, pricking, itching.
- Describe what makes the pain worse and what relieves the pain.
- Use of tools to determine the intensity of pain.
- Using pain scales you can rate your pain by relating to the assessment tools.



Using pain diagrams you can locate your pain .



Using pain scales (0-10) you can rate your pain.

Using the faces you can classify your pain.

Pain Management

Pain is managed by using a ladder developed by World Health Organisation. After locating the pain and assessing the pain, classify it as mild, moderate or severe. The World Health Organisation management guides which treatment to use after classification of pain.

World Health Organisation pain management ladder

Step 1 is mild pain which ranges from 0-3 on the universal assessment scale on for this type of pain we use paracetamol (Panado) 2 tablets, 4 times in a day. You can also use Asprin 2 tablets, 4 times a day.

Step 2 is moderate pain which ranges from 4-6 on the universal assessment scale and for this type of pain we use Diclofenac 1 tablet, 4 times in a day or you may use codeine 1 tablet or 2 tablets, 4 times in a day.

Step 3 is severe pain which ranges from 7-10 on the universal scale. Here we use Morphine. It is either in tablet or solution form. If it is tablets form you take 2 tablets 6 times in a day if in solution form then 2 tea spoons 6 times in a day.

Make sure that you take the drugs at the required time, do not wait for the pain to come, and do not stop taking the drugs if you are not feeling pain, you need to take them all any time according to prescription because if you stop taking them, then the pain will come again.

Misconceptions about your pain and pain medication

Patients exaggerate the pain.

Patients need to experience the pain.

Patients should not continuously take pain medication because they will become addicted.

Good patients do not complain about their pain.

Important points to remember

Pain can be controlled and managed with drugs.

Patients have the right to complain about their pain.

Patients should talk to the doctor or nurse as soon as pain begins.

Patients have the right to pain control.

Patients should not let fear keep them in pain.

Patients have the right to appropriate assessment and management of pain.
All HIV/AIDS patients can live a pain free life.

Pain medication should be given using the following principles:

By the mouth Giving pain medication by mouth is the simplest and most reliable method for most patients. Dissolve the tablets in water if the patient has mouth sores for easy swallowing.

By the clock Constant pain needs regular pain medication to keep it away. Pain that is allowed to build up is more difficult to control. Do not wait for the pain to return but give pain medication at regular intervals according to their duration of action.

By the ladder The World Health Organisation pain management ladder gives a logical way of increasing the strength of pain medication in steps as pain increases.

Other ways of managing pain.

You also need to do the following when in pain to distract it apart from taking the drugs:

- Apply warm compress on the site where there is pain.
- Take warm fluids when feeling abdominal pains.
- Wash your mouth with salty water every day 4 times in a day if you have oral sores.
- Read a newspaper, magazine or this booklet if in pain or any reading material you find interesting like Bible, Quran.
- Play soft music or tell stories to the patient.
- Give gentle massage on the area where patient feels pain.
- Perform relaxation exercises like deep breathing regularly.
- Elevate feet's and legs if they are swollen.
- Seek pastoral support and prayer.

References

APCA (2008) A palliative care training manual: community based male caregivers in Africa

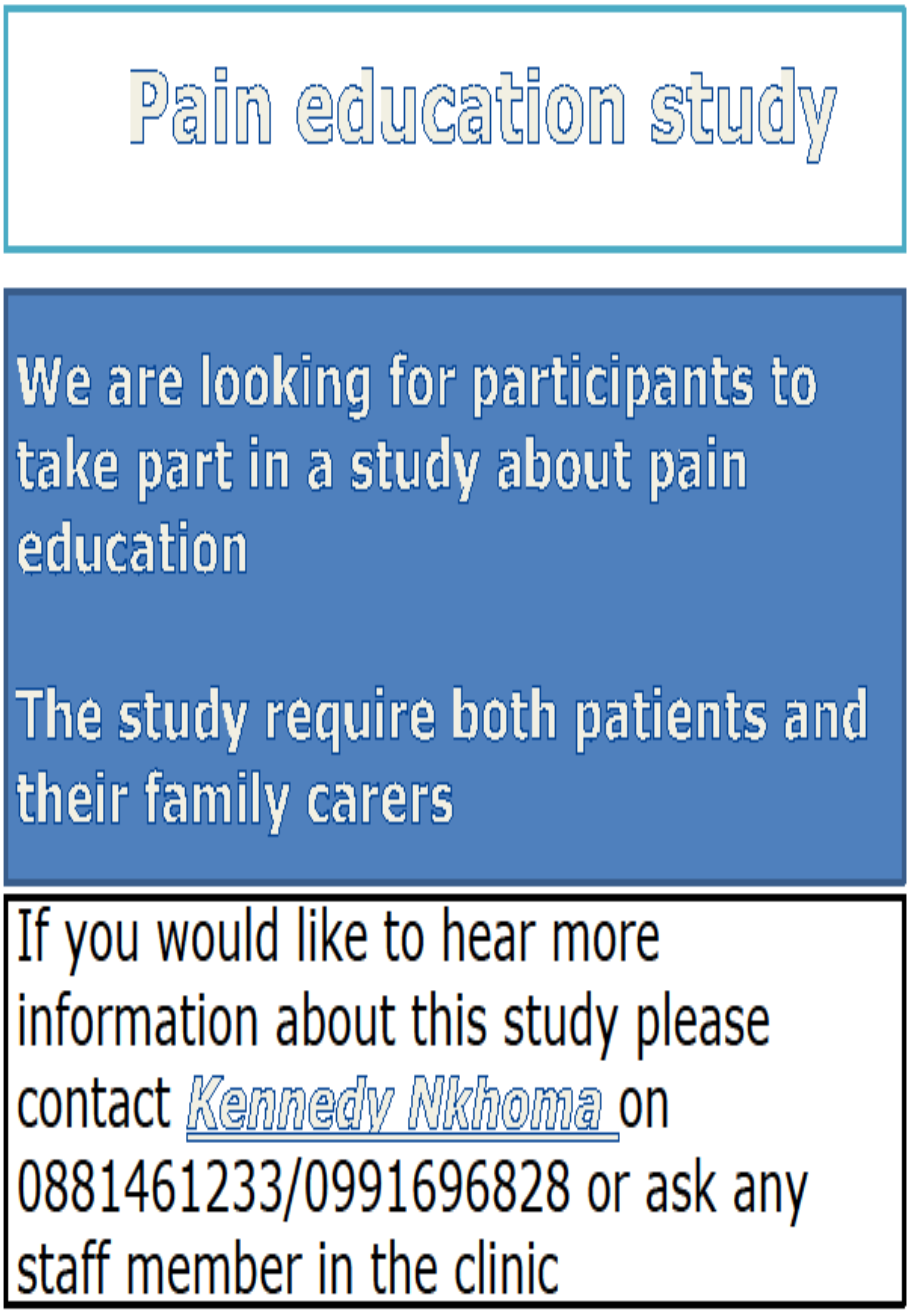
PACAM (2008) Palliative care A field guide for community home-based care volunteers

The Worldwide palliative care alliance (2008) Palliative care tool kit

WHO (2006) Caregiver booklet: symptom management and end of life care

Contact person: Kennedy Nkhoma on 0991696828/0888715056

Appendix 14 Poster



Kafukufuku wa Ulwilwi wa muthupi

Tikupanga kafukufuku wakukhwaksa ulwilwi wa muthupi

Tikukhumba balwali pamoza na bawovwili bawo

Pala mukukhumba kupulika mwa chisani sani chonde kumanani na Kennedy Nkhoma panji yimbani pa 0881461233/0991696828 panyakhe fumbani kwa wali yose uyo wakugwira ntchito pa chipatala pano

Appendix 15 Stata 'do' files

Organisation of variables and generation of derived variables

```
*CONVENTIONS

*Rename variables: PB=Patient before CB=Carer before PF=Patient follow-up
CF=Carer follow-up DE=Demog DA=Dates

*Value label sets end with vals e.g. relvals

*Collapsed variables end with COLL


*Patient before BPI renaming variables

*Note BPI question 1 are string and we possibly want them to be binary yes/no
variables


*BPIQ6 is also string, may need to create a numerical variable (receiving meds
yes/no) and then think about other

*variables that capture what they are taking, let's discuss

*19/10 KN working on this with treatment do file

rename  Area11          BPIA1_PB

rename  Area21          BPIA2_PB

rename  Area31          BPIA3_PB

rename  Area41          BPIA4_PB

rename  Area51          BPIA5_PB

rename  Area61          BPIA6_PB

rename  Area71          BPIA7_PB

rename  Area81          BPIA8_PB

rename  Q2Painworst1      BPIQ2_PB

rename  Q3Painleast1      BPIQ3_PB

rename  Q4Painaverage1  BPIQ4_PB

rename  Q5Painrightnow1 BPIQ5_PB

rename  Q6Treatment1      BPIQ6_PB

rename  Q7Painreliefge1   BPIQ7_PB
```

```
rename  Q8aPaininterf~1  BPIQ8aPB

rename  Q8bMood1         BPIQ8bPB

rename  Q8cwalking1      BPIQ8cPB

rename  Q8dwork1         BPIQ8dPB

rename  Q8erelationsh~1  BPIQ8ePB

rename  Q8fsleep1        BPIQ8fPB

rename  Q8genjoyment1    BPIQ8gPB


*Patient before BPI applying variable labels

label variable BPIA1_PB "Baseline BPI Question 1 head/neck pain"

label variable BPIA2_PB "Baseline BPI Question 1 Right arm pain"

label variable BPIA3_PB "Baseline BPI Question 1 Left arm pain"

label variable BPIA4_PB "Baseline BPI Question 1 Chest pain"

label variable BPIA5_PB "Baseline BPI Question 1 Abdominal pain"

label variable BPIA6_PB "Baseline BPI Question 1 Right leg pain"

label variable BPIA7_PB "Baseline BPI Question 1 Left leg pain"

label variable BPIA8_PB "Baseline BPI Question 1 Back pain"

label variable BPIQ2_PB   "Baseline BPI Question 2 Worst pain"

label variable BPIQ3_PB   "Baseline BPI Question 3 Pain least"

label variable BPIQ4_PB   "Baseline BPI Question 4 average pain"

label variable BPIQ5_PB   "Baseline BPI Question 5 current pain"

label variable BPIQ6_PB   "Baseline BPI Question 6 pain treatment"

label variable BPIQ7_PB   "Baseline BPI Question 7 pain relief %ge"

label variable BPIQ8aPB "Baseline BPI Question 8a pain & activity"

label variable BPIQ8bPB "Baseline BPI Question 8b pain & mood"

label variable BPIQ8cPB "Baseline BPI Question 8c pain & walking"

label variable BPIQ8dPB "Baseline BPI Question 8d pain & work"

label variable BPIQ8ePB "Baseline BPI Question 8e pain & relationships"

label variable BPIQ8fPB "Baseline BPI Question 8f pain & sleep"

label variable BPIQ8gPB "Baseline BPI Question 8g pain & enjoyment"
```

```
*PPQ patient before

*rename PPQ patient before variables

rename  HIVAIDSpainca~1PPQ1_PB

rename  Q9Painmedicin~1 PPQ2_PB

rename  Q10Painmedici~1 PPQ3_PB

rename  Q11largerdose~1 PPQ4_PB

rename  Q12Painmedici~1 PPQ5_PB

rename  Q13Nonpharmac~1PPQ6_PB

rename  Q14Painmedici~1 PPQ7_PB

rename  Q15Patientsar~1  PPQ8_PB

rename  Q16Worstpainw~1PPQ9_PB

rename  Q16Painlastwe~1 PPQ10_PB

rename  Q17Painnow1      PPQ11_PB

rename  Q18Painrelief1     PPQ12_PB

rename  Q19Paindistre~1  PPQ13_PB

rename  Q20Paindistre~1  PPQ14_PB

rename  Q21Paincontro~1 PPQ15_PB

rename  Q22Futurepain1   PPQ16_PB


*Patient before PPQ applying variable labels

label variable PPQ1_PB "Baseline PPQ Question 1 HIV/AIDS pain can be relieved"

label variable PPQ2_PB "Baseline PPQ Question 2 pain medication only when pain is
severe"

label variable PPQ3_PB "Baseline PPQ Question 3 patients become addicted to
medication"

label variable PPQ4_PB "Baseline PPQ Question 4 larger doses for worse pain"

label variable PPQ5_PB "Baseline PPQ Question 5 pain medication and timing"

label variable PPQ6_PB "Baseline PPQ Question 6 non-pharmacological interventions"

label variable PPQ7_PB "Baseline PPQ Question 7 pain medication interfere with
breathing"
```

```
label variable PPQ8_PB "Baseline PPQ Question 8 patients are often given too much pain medication"

label variable PPQ9_PB "Baseline PPQ Question 9 worse pain means worse HIV/AIDS"

label variable PPQ10_PB   "Baseline PPQ Question 10 pain last week"

label variable PPQ11_PB   "Baseline PPQ Question 11 pain now"

label variable PPQ12_PB   "Baseline PPQ Question 12 pain relief"

label variable PPQ13_PB   "Baseline PPQ Question 13 pain distress to patient"

label variable PPQ14_PB   "Baseline PPQ Question 14 pain distress to family"

label variable PPQ15_PB   "Baseline PPQ Question 15 pain control ability"

label variable PPQ16_PB   "Baseline PPQ Question 16 future pain"


*POS patient before

*Renaming variables

rename  Q23Painrating~1 POSQ1_PB

rename  Q24othersympt~1         POSQ2_PB

rename  Q25Worryabout~1         POSQ3_PB

rename  Q26Sharingoff~1 POSQ4_PB

rename  Q27Lifeworthw~1POSQ5_PB

rename  Q28Feelingpea~1POSQ6_PB

rename  Q29Helpandadv~1         POSQ7_PB


*POS patient before

*Applying variable labels

label variable POSQ1_PB   "Baseline POS Question 1 pain rating last three days"

label variable POSQ2_PB   "Baseline POS Question 2 other symptoms last three days"

label variable POSQ3_PB   "Baseline POS Question 3 worry about illness last three days"

label variable POSQ4_PB   "Baseline POS Question 4 sharing of feelings"

label variable POSQ5_PB   "Baseline POS Question 5 life worthfulness"

label variable POSQ6_PB   "Baseline POS Question 6 feeling peace"

label variable POSQ7_PB   "Baseline POS Question 7 help and advice"
```

```
*Renaming Patient identifiable variables including allocation

*Source of referral will need encoding - KN to do this from spreadsheet.

*Drop trial status

rename  Patientname1  PN_PB

rename  Address1  Address_PB

rename  Nameofcarer1  CN_PB

rename  sourceofrefer~1  SOR_PB

rename  relationship1 Rel_PCB

rename  Allocation1  A_PB

rename  Statusofthetr~1  TS_PCB

rename  Sitecentre1  SC_PCB

drop TS_PCB


*Applying labels to patient identifying variables

label variable PN_PB"Baseline patient name"

label variable Address_PB "Baseline patient address"

label variable CN_PB"Baseline carer name"

label variable SOR_PB"Baseline referring centre"

label variable A_PB "Baseline patient group allocation"

label variable Rel_PCB "carer relationship to the patient"

label variable SC_PCB "Baseline recruitment centre"


*Decided to drop BP1 BR1 BS1 BT1 re text information about assessment and
telephone call

drop BP1 BR1 BS1 BT1

*FPQ carer before

*rename FPQ carer before variables

rename  Q1Paincanbere~2FPQ1_CB

rename  Q2Painmedicin~2FPQ2_CB

rename  Q3Painmedicin~2FPQ3_CB
```

```
rename  Q4largerdoses~2 FPQ4_CB

rename  Q5Painmedicin~2 FPQ5_CB

rename  Q6Nonpharmaco~2 FPQ6_CB

rename  Q7Painmedicin~2 FPQ7_CB

rename  Q8Patientsare~2  FPQ8_CB

rename  Q9Worstpainwo~2 FPQ9_CB

rename  Q10painlastwe~2 FPQ10_CB

rename  Q11Painnow2 FPQ11_CB

rename  Q12Painrelief2 FPQ12_CB

rename  Q13Paindistre~2  FPQ13_CB

rename  Q14Paindistre~2  FPQ14_CB

rename  Q15Paincontro~2 FPQ15_CB

rename  Q16Futurepain2   FPQ16_CB


*FPQ carer before

*Applying variable labels

label variable FPQ1_CB     "Baseline FPQ Question 1 HIV/AIDS pain can be relieved"

label variable FPQ2_CB     "Baseline FPQ Question 2 pain medication and pain
severity"

label variable FPQ3_CB     "Baseline FPQ Question 3 pain medicine and addiction"

label variable FPQ4_CB     "Baseline FPQ Question 4 larger doses for worst pain"

label variable FPQ5_CB     "Baseline FPQ Question 5 pain medicine and timing"

label variable FPQ6_CB     "Baseline FPQ Question 6 non-pharmacological
interventions"

label variable FPQ7_CB     "Baseline FPQ Question 7 pain medicine and breathing"

label variable FPQ8_CB     "Baseline FPQ Question 8 patients are often given too
much pain medicine"

label variable FPQ9_CB     "Baseline FPQ Question 9 worst pain=worst HIV/AIDS"

label variable FPQ10_CB    "Baseline FPQ Question 10 pain last week"

label variable FPQ11_CB    "Baseline FPQ Question 11 pain now"

label variable FPQ12_CB    "Baseline FPQ Question 12 pain relief"

label variable FPQ13_CB    "Baseline FPQ Question 13 pain distress to patient"
```

```
label variable FPQ14_CB    "Baseline FPQ Question 14 pain distress to carer"

label variable FPQ15_CB    "Baseline FPQ Question 15 pain control ability"

label variable FPQ16_CB    "Baseline FPQ Question 16 future pain"


*PCRS carer before

*rename PCRS carer before variables

rename  Q17Godwillble~2 PCRSQ1_CB

rename  Q18Selffeeling2   PCRSQ2_CB

rename  Q19Feelingstr~2  PCRSQ3_CB

rename  Q20Otherssay2    PCRSQ4_CB

rename  Q21Someonewil~2 PCRSQ5_CB

rename  Q22Receivings~2 PCRSQ6_CB

rename  Q23Closerrela~2  PCRSQ7_CB

rename  Q24Newinforma~2 PCRSQ8_CB

rename  Q25Newwaysofc~2 PCRSQ9_CB

rename  Q26Newfriends2  PCRSQ10_CB

rename  Q27Feelingmor~2 PCRSQ11_CB

rename  Q28Freedomtom~2 PCRSQ12_CB

rename  Q29receptionf~2  PCRSQ13_CB

rename  Q30feelinghap~2 PCRSQ14_CB

rename  Q31Feelingfam~2 PCRSQ15_CB

rename  Q32Familyloop~2PCRSQ16_CB


*PCRS carer before

*apply PCRS carer variable labels

label variable PCRSQ1_CB "Baseline PCRS Question 1 God will bless me"

label variable PCRSQ2_CB "Baseline PCRS Question 2 better self feeling"

label variable PCRSQ3_CB "Baseline PCRS Question 3feeling stronger and tolerant"

label variable PCRSQ4_CB "Baseline PCRS Question 4 caring is right thing"

label variable PCRSQ5_CB "Baseline PCRS Question 5 someone will care for me"
```

```
label variable PCRSQ6_CB "Baseline PCRS Question 6 smile, touch eye contact is
important"

label variable PCRSQ7_CB "Baseline PCRS Question 7 closer relationship"

label variable PCRSQ8_CB "Baseline PCRS Question 8 new information"

label variable PCRSQ9_CB "Baseline PCRS Question 9 news caring ways"

label variable PCRSQ10_CB "Baseline PCRS Question 10 new friends"

label variable PCRSQ11_CB "Baseline PCRS Question 11 feeling more important"

label variable PCRSQ12_CB "Baseline PCRS Question 12 decisions"

label variable PCRSQ13_CB "Baseline PCRS Question 13 health care workers
reception"

label variable PCRSQ14_CB "Baseline PCRS Question 14 feeling happier"

label variable PCRSQ15_CB "Baseline PCRS Question 15 family growth"

label variable PCRSQ16_CB "Baseline PCRS Question 16 Family looks up to me"


*POS carer before

*rename POS carer before variables

rename  Q33Informatio~2 POSQ8_CB

rename  Q34Confidence2  POSQ9_CB

rename  Q35familyworr~2 POSQ10_CB


*POS carer before

*apply POS carer variable labels

label variable POSQ8_CB   "Baseline POS Question 8 information"

label variable POSQ9_CB   "Baseline POS Question 9 confidence"

label variable POSQ10_CB "Baseline POS Question 10 family worries"


* Rename and label Allocation variable from carers before dataset

* Need to check whether same as before

rename  Allocation2  A_CB

label variable A_CB "Baseline carer group allocation"
```

*Patient after BPI renaming variables

*As before BPI question 1 are string and we possibly want them to be binary yes/no variables, not urgent, let's discuss

*BPIQ6 is also string, may need to create a numerical variable (receiving meds yes/no) and then think about other

*variables that capture what they are taking, let's discuss

```
rename  Area13          BPIA1_PF

rename  Area23          BPIA2_PF

rename  Area33          BPIA3_PF

rename  Area43          BPIA4_PF

rename  Area53          BPIA5_PF

rename  Area63          BPIA6_PF

rename  Area73          BPIA7_PF

rename  Area83          BPIA8_PF

rename  Q2Painworst3      BPIQ2_PF

rename  Q3Painleast3      BPIQ3_PF

rename  Q4Painaverage3  BPIQ4_PF

rename  Q5Painrightnow3 BPIQ5_PF

rename  Q6Treatment3      BPIQ6_PF

rename  Q7Painreliefge3   BPIQ7_PF

rename  Q8aPaininterf~3  BPIQ8a_PF

rename  Q8bMood3          BPIQ8b_PF

rename  Q8cwalking3       BPIQ8c_PF

rename  Q8dwork3          BPIQ8d_PF

rename  Q8erelationsh~3  BPIQ8e_PF

rename  Q8fsleep3         BPIQ8f_PF

rename  Q8genjoyment3   BPIQ8g_PF
```

*Patient after BPI applying variable labels

```
label variable BPIA1_PF "Follow-up BPI Question 1 head/neck pain"
```

```
label variable BPIA2_PF "Follow-up BPI Question 1 Right arm pain"

label variable BPIA3_PF "Follow-up BPI Question 1 Left arm pain"

label variable BPIA4_PF "Follow-up BPI Question 1 Chest pain"

label variable BPIA5_PF "Follow-up BPI Question 1 Abdominal pain"

label variable BPIA6_PF "Follow-up BPI Question 1 Right leg pain"

label variable BPIA7_PF "Follow-up BPI Question 1 Left leg pain"

label variable BPIA8_PF "Follow-up BPI Question 1 Back pain"

label variable BPIQ2_PF    "Follow-up BPI Question 2 Worst pain"

label variable BPIQ3_PF    "Follow-up BPI Question3 Pain least"

label variable BPIQ4_PF    "Follow-up BPI Question 4 average pain"

label variable BPIQ5_PF    "Follow-up BPI Question 5 current pain"

label variable BPIQ6_PF "Follow-up BPI Question 6 pain treatment"

label variable BPIQ7_PF    "Follow-up BPI Question 7 pain relief %ge"

label variable BPIQ8a_PF "Follow-up BPI Question 8 pain and activity"

label variable BPIQ8b_PF "Follow-up BPI Question 8b pain & mood"

label variable BPIQ8c_PF "Follow-up BPI Question 8c pain & walking"

label variable BPIQ8d_PF "Follow-up BPI Question 8d pain & work"

label variable BPIQ8e_PF "Follow-up BPI Question 8e pain & relationships"

label variable BPIQ8f_PF "Follow-up BPI Question 8f pain & sleep"

label variable BPIQ8g_PF "Follow-up BPI Question 8g pain & enjoyment"


*PPQ patient after

*rename PPQ patient before variables

rename  HIVAIDSpainca~3 PPQ1_PF

rename  Q9Painmedicin~3 PPQ2_PF

rename  Q10Painmedici~3 PPQ3_PF

rename  Q11largerdose~3 PPQ4_PF

rename  Q12Painmedici~3 PPQ5_PF

rename  Q13Nonpharmac~3 PPQ6_PF

rename  Q14Painmedici~3 PPQ7_PF
```

```
rename  Q15Patientsar~3 PPQ8_PF

rename  Q16Worstpainw~3 PPQ9_PF

rename  Q16Painlastwe~3 PPQ10_PF

rename  Q17Painnow3 PPQ11_PF

rename  Q18Painrelief3 PPQ12_PF

rename  Q19Paindistre~3  PPQ13_PF

rename  Q20Paindistre~3  PPQ14_PF

rename  Q21Paincontro~3 PPQ15_PF

rename  Q22Futurepain3   PPQ16_PF


*Patient after PPQ applying variable labels

label variable PPQ1_PF "Follow-up PPQ Question 1 HIV/AIDS pain can be relieved"

label variable PPQ2_PF "Follow-up PPQ Question 2 pain medication only when pain is
severe"

label variable PPQ3_PF "Follow-up PPQ Question 3 patients become addicted to
medication"

label variable PPQ4_PF "Follow-up PPQ Question 4 larger doses for worse pain"

label variable PPQ5_PF "Follow-up PPQ Question 5 pain medication and timing"

label variable PPQ6_PF "Follow-up PPQ Question 6 non-pharmacological
interventions"

label variable PPQ7_PF "Follow-up PPQ Question 7 pain medication interfere with
breathing"

label variable PPQ8_PF "Follow-up PPQ Question 8 patients are often given too much
pain medication"

label variable PPQ9_PF "Follow-up PPQ Question 9 worse pain means worse
HIV/AIDS"

label variable PPQ10_PF "Follow-up PPQ Question 10 pain last week"

label variable PPQ11_PF    "Follow-up PPQ Question 11 pain now"

label variable PPQ12_PF    "Follow-up PPQ Question 12 pain relief"

label variable PPQ13_PF    "Follow-up PPQ Question 13 pain distress to patient"

label variable PPQ14_PF    "Follow-up PPQ Question 14 pain distress to family"

label variable PPQ15_PF    "Follow-up PPQ Question 15 pain control ability"

label variable PPQ16_PF    "Follow-up PPQ Question 16 future pain"
```

```
*POS patient after

*Renaming variables

rename  Q23Painrating~3 POSQ1_PF

rename  Q24othersympt~3 POSQ2_PF

rename  Q25Worryabout~3 POSQ3_PF

rename  Q26Sharingoff~3 POSQ4_PF

rename  Q27Lifeworthw~3POSQ5_PF

rename  Q28Feelingpea~3POSQ6_PF

rename  Q29Helpandadv~3 POSQ7_PF


*POS patient after

*Applying variable labels

label variable POSQ1_PF   "Follow-up POS Question 1 pain rating last three days"

label variable POSQ2_PF   "Follow-up POS Question 2 other symptoms last three
days"

label variable POSQ3_PF   "Follow-up POS Question 3 worry about illness last three
days"

label variable POSQ4_PF   "Follow-up POS Question 4 sharing of feelings"

label variable POSQ5_PF   "Follow-up POS Question 5 life worthfulness"

label variable POSQ6_PF   "Follow-up POS Question 6 feeling peace"

label variable POSQ7_PF   "Follow-up POS Question 7 help and advice"


*Renaming Patient identifiable variables including allocation from patient after

drop Statusofthetr~3

rename  Patientname3  PN_PF

rename  Address3  Address_PF

rename  Nameofcarer3  CN_PF

rename  BC3  Address_CF

rename  sourceofrefer~3  SOR_PF

rename  relationship3 Rel_CF

rename  Allocation3  A_PF
```

```
rename  Sitecentre3  SC_PCF

*This variable 'as patient' for all participants:
drop Address_CF

*Applying labels to patient after identifying variables
label variable PN_PF "Follow-up patient name"
label variable Address_PF "Follow-up patient address"
label variable CN_PF "Follow-up carer name"
label variable SOR_PF "F/up referring centre"
label variable Rel_CF "F/up carer relationship to the patient"
label variable A_PF "Follow-up patient group allocation"
label variable SC_PCF "F/up recruitment centre"

*FPQ carer after
*rename FPQ carer after variables
rename  Q1Paincanbere~4FPQ1_CF
rename  Q2Painmedicin~4 FPQ2_CF
rename  Q3Painmedicin~4 FPQ3_CF
rename  Q4largerdoses~4 FPQ4_CF
rename  Q5Painmedicin~4 FPQ5_CF
rename  Q6Nonpharmaco~4 FPQ6_CF
rename  Q7Painmedicin~4 FPQ7_CF
rename  Q8Patientsare~4  FPQ8_CF
rename  Q9Worstpainwo~4 FPQ9_CF
rename  Q10painlastwe~4 FPQ10_CF
rename  Q11Painnow4 FPQ11_CF
rename  Q12Painrelief4 FPQ12_CF
rename  Q13Paindistre~4  FPQ13_CF
rename  Q14Paindistre~4  FPQ14_CF
```

```
rename  Q15Paincontro~4 FPQ15_CF

rename  Q16Futurepain4   FPQ16_CF


*FPQ carer after

*Applying variable labels

label variable FPQ1_CF "Follow-up FPQ Question 1 HIV/AIDS pain can be relieved"

label variable FPQ2_CF "Follow-up FPQ Question 2 pain medication and pain severity"

label variable FPQ3_CF "Follow-up FPQ Question 3 pain medicine and addiction"

label variable FPQ4_CF "Follow-up FPQ Question 4 larger doses for worst pain"

label variable FPQ5_CF "Follow-up FPQ Question 5 pain medicine and timing"

label variable FPQ6_CF "Follow-up FPQ Question 6 non-pharmacological
interventions"

label variable FPQ7_CF "Follow-up FPQ Question 7 pain medicine and breathing"

label variable FPQ8_CF "Follow-up FPQ Question 8 patients are often given too much
pain medicine"

label variable FPQ9_CF "Follow-up FPQ Question 9 worst pain=worst HIV/AIDS"

label variable FPQ10_CF "Follow-up FPQ Question 10 pain last week"

label variable FPQ11_CF    "Follow-up FPQ Question 11 pain now"

label variable FPQ12_CF    "Follow-up FPQ Question 12 pain relief"

label variable FPQ13_CF    "Follow-up FPQ Question 13 pain distress to patient"

label variable FPQ14_CF    "Follow-up FPQ Question 14 pain distress to carer"

label variable FPQ15_CF    "Follow-up FPQ Question 15 pain control ability"

label variable FPQ16_CF    "Follow-up FPQ Question 16 future pain"


*PCRS carer after

*rename PCRS carer after variables

rename  Q17Godwillble~4 PCRSQ1_CF

rename  Q18Selffeeling4   PCRSQ2_CF

rename  Q19Feelingstr~4  PCRSQ3_CF

rename  Q20Otherssay4    PCRSQ4_CF

rename  Q21Someonewil~4          PCRSQ5_CF
```

```
rename  Q22Receivings~4 PCRSQ6_CF

rename  Q23Closerrela~4  PCRSQ7_CF

rename  Q24Newinforma~4 PCRSQ8_CF

rename  Q25Newwaysofc~4 PCRSQ9_CF

rename  Q26Newfriends4  PCRSQ10_CF

rename  Q27Feelingmor~4 PCRSQ11_CF

rename  Q28Freedomtom~4 PCRSQ12_CF

rename  Q29receptionf~4  PCRSQ13_CF

rename  Q30feelinghap~4 PCRSQ14_CF

rename  Q31Feelingfam~4 PCRSQ15_CF

rename  Q32Familyloop~4PCRSQ16_CF


*PCRS carer after

*apply PCRS carer after variable labels

label variable PCRSQ1_CF "Follow-up PCRS Question 1 God will bless me"

label variable PCRSQ2_CF "Follow-up PCRS Question 2 better self feeling"

label variable PCRSQ3_CF "Follow-up PCRS Question 3feeling stronger and tolerant"

label variable PCRSQ4_CF "Follow-up PCRS Question 4 caring is right thing"

label variable PCRSQ5_CF "Follow-up PCRS Question 5 someone will care for me"

label variable PCRSQ6_CF "Follow-up PCRS Question 6 smile, touch eye contact is
important"

label variable PCRSQ7_CF "Follow-up PCRS Question 7 closer relationship"

label variable PCRSQ8_CF "Follow-up PCRS Question 8 new information"

label variable PCRSQ9_CF "Follow-up PCRS Question 9 news caring ways"

label variable PCRSQ10_CF "Follow-up PCRS Question 10 new friends"

label variable PCRSQ11_CF "Follow-up PCRS Question 11 feeling more important"

label variable PCRSQ12_CF "Follow-up PCRS Question 12 decisions"

label variable PCRSQ13_CF "Follow-up PCRS Question 13health care workers
reception"

label variable PCRSQ14_CF "Follow-up PCRS Question 14 feeling happier"

label variable PCRSQ15_CF "Follow-up PCRS Question 15 family growth"
```

```
label variable PCRSQ16_CF "Follow-up PCRS Question 16 Family looks up to me"

*POS carer after
*rename POS carer after variables
rename  Q33Informatio~4 POSQ8_CF
rename  Q34Confidence4  POSQ9_CF
rename  Q35familyworr~4 POSQ10_CF

*POS carer after
*apply POS carer variable labels
label variable POSQ8_CF   "Follow-up POS Question 8 information"
label variable POSQ9_CF   "Follow-up POS Question 9 confidence"
label variable POSQ10_CF "Follow-up POS Question 10 family worries"

*Carer follow-up ID variables
rename  Allocation4 A_CF
label variable A_CF "Follow-up carer group allocation"

*Demographic and ID variables from Copy of Gender file
*Rename
rename  Patientname5      PN_DE
rename  GenPt5            PG_DE
rename  Nameofcarer5      CN_DE
rename  GenCarer5         CG_DE
rename  relationship5     RELST_DE
rename  Relationship5     REL_DE
rename  Ptmaritalstat~5   PMARITAL_DE
rename  Carersmarital~5   CMARITAL_DE
rename  Patienteducat~5   PE_DE
rename  Carerseducati~5   CE_DE
```

```
rename  Patientreligi~5     PR_DE
rename  Carerreligion5      CR_DE
rename  Patientoccupa~5  PO_DE
rename  Careroccupati~5  CO_DE

*This string variable checked 12/10/13 and does not add anything to REL_DE
drop RELST_DE

*Demographic and ID variables from Copy of Gender file
*Label variables
label variable PN_DE        "patient name"
label variable PG_DE        "patient gender"
label variable CN_DE        "carer name"
label variable CG_DE        "carer gender"
label variable REL_DE       "Carers relationship to the patient"
label variable PMARITAL_DE "patient marital status"
label variable CMARITAL_DE "carer marital status"
label variable PE_DE        "patient education"
label variable CE_DE        "carer education"
label variable PR_DE        "patient religion"
label variable CR_DE        "carer religion"
label variable PO_DE        "patient occ"
label variable CO_DE        "carer occ"
label define genvals 0 "Male" 1 "Female"
label values PG_DE CG_DE genvals
label define edvals 1 "Primary school" 2 "Secondary school" 3 "College/University"
label values PE_DE CE_DE edvals
label define relnvals 1 "Christianity" 2" Muslim"
label values PR_DE CR_DE relnvals
*Date variables from New Dates (2) and dates2.do
```

```
*Rename
rename dobp DOBP_DA
rename dobc DOBC_DA
rename doia DOIA_DA
rename doc  DOC_DA
rename dop  DOP_DA
rename dofs DOFS_DA
rename dofa DOFA_DA

*Date variables
*Apply labels
label variable DOBP_DA "Patient date of birth"
label variable DOBC_DA "Carer date of birth"
label variable DOIA_DA "Date of initial approach"
label variable DOC_DA "Date of consent"
label variable DOP_DA "Date of phone contact"
label variable DOFS_DA "Date of scheduled follow-up"
label variable DOFA_DA "Date of actual follow-up"

*Generate Patient Attrition codes
gen p_attrition=0
recode p_attrition 0=3 if IDNumber==25
recode p_attrition 0=4 if IDNumber==26
recode p_attrition 0=3 if IDNumber==42
recode p_attrition 0=4 if IDNumber==69
recode p_attrition 0=3 if IDNumber==73
recode p_attrition 0=3 if IDNumber==75
recode p_attrition 0=1 if IDNumber==83
recode p_attrition 0=1 if IDNumber==84
recode p_attrition 0=3 if IDNumber==86
```

```
recode p_attrition 0=1 if IDNumber==89

recode p_attrition 0=4 if IDNumber==94

recode p_attrition 0=2 if IDNumber==102

recode p_attrition 0=5 if IDNumber==103

recode p_attrition 0=1 if IDNumber==148

recode p_attrition 0=2 if IDNumber==186


*Apply patient attrition value and variable labels

label define pattvals 0 "Followed-up" 1 "Patient died" 2 "No transport" 3 "Moved
away" 4 "Not traceable" 5 "Patient unwell"

label values p_attrition pattvals

label variable p_attrition "patient attrition"


*Generate Carer Attrition codes

gen c_attrition=0

recode c_attrition 0=2 if IDNumber==17

recode c_attrition 0=3 if IDNumber==25

recode c_attrition 0=4 if IDNumber==26

recode c_attrition 0=2 if IDNumber==40

recode c_attrition 0=3 if IDNumber==42

recode c_attrition 0=5 if IDNumber==48

recode c_attrition 0=4 if IDNumber==69

recode c_attrition 0=2 if IDNumber==70

recode c_attrition 0=2 if IDNumber==72

recode c_attrition 0=3 if IDNumber==73

recode c_attrition 0=3 if IDNumber==75

recode c_attrition 0=1 if IDNumber==83

recode c_attrition 0=1 if IDNumber==84

recode c_attrition 0=3 if IDNumber==86

recode c_attrition 0=1 if IDNumber==89

recode c_attrition 0=4 if IDNumber==94
```

```
recode c_attrition 0=2 if IDNumber==102

recode c_attrition 0=6 if IDNumber==103

recode c_attrition 0=2 if IDNumber==104

recode c_attrition 0=2 if IDNumber==110

recode c_attrition 0=5 if IDNumber==118

recode c_attrition 0=5 if IDNumber==128

recode c_attrition 0=1 if IDNumber==148

recode c_attrition 0=2 if IDNumber==186

recode c_attrition 0=5 if IDNumber==190


*Apply carer attrition value and variable labels

label define cattvals 0 "Followed-up" 1 "Patient died" 2 "No transport" 3 "Moved
away" 4 "Not traceable" 5 "Too busy" 6 "Patient unwell" , replace

label values c_attrition cattvals

label variable c_attrition "carer attrition"


*Apply labels to carer relationship and create new collapsed variable

label define relvals 1 "Husband" 2 "Wife" 3 "Sister" 4 "Brother" 5 "Son" 6 "Daughter"
7" Friend" 8 "Mother" 9 "Father" 10 "Cousin"  11 "Aunt" 12 "Grandmother" 13
"Sister-in law"

label values REL_DE relvals

gen RELCOLL=REL_DE

recode RELCOLL 1=1 2=1 3=2 4=2 5=3 6=3 7=4 8=5 9=5 10=6 11=6 12=6 13=6

label define relcvals 1 "Spouse" 2 "Sibling" 3 "Son/daughter" 4 "Friend" 5 " Parent" 6
" Other relative", replace

label values RELCOLL relcvals

label variable RELCOLL "Carer relationship to patient"


*Create and code a variable for patient marital status (collapsed)

gen PMARCOLL= PMARITAL_DE

recode PMARCOLL 1=1 2=2 3=3 4=4 5=4

label define marvals 1"Single" 2 "Married" 3 "Divorced/separated" 4
"Widow/widower", replace
```

```
label values PMARCOLL marvals

label var PMARCOLL "Patient marital status"


*Checked crosstabs OK 12/10/13

drop PMARITAL_DE


*Create and code a variable for carer marital status (collapsed)

gen CMARCOLL=CMARITAL_DE

recode CMARCOLL 1=1 2=2 3=3 4=4 5=4

label values CMARCOLL marvals

label var CMARCOLL "Carer marital status"


*Checked crosstabs OK 12/10/13

drop CMARITAL_DE


*Create and code a variable for patient occupation (collapsed)

gen POCCOLL=PO_DE

recode POCCOLL 1=1 2=2 6=2 3=3 7=4 9=5 12=6 13=6 14=6 15=6 18=7 4=10
5=10 8=9 10=8 11=10 16=10 17=10 18=7 19=2 20=10 21=8 22=6

label define occvals 1"Farmer" 2"Civil servant" 3"Housewife" 4"Unemployed"
5"Student" 6"Skilled manual" 7"Retired" 8"Admin workers" 9"Small scale business"
10"Other", replace

label values POCCOLL occvals

label variable POCCOLL "Patient occupation




*Don't wish to get rid of PO_DE at this stage as 'other' category is so large. Can we
think about this again?


*Create and code a variable for carer occupation (collapsed)

gen COCOLL=CO_DE
```

```
recode COCOLL 1=1 2=2 6=2 3=3 7=4 9=5 12=6 13=6 14=6 15=6 18=7 4=10
5=10 8=9 10=8 11=10 16=10 17=10 18=7 19=2 20=10 21=8 22=6

label values COCOLL occvals

label variable COCOLL "Carer occupation"


* variable for coinfection

gen cormobidity=0

recode cormobidity 0=2 if IDNumber==41

recode cormobidity 0=1 if IDNumber==47

recode cormobidity 0=1 if IDNumber==50

recode cormobidity 0=1 if IDNumber==54

recode cormobidity 0=1 if IDNumber==55

recode cormobidity 0=1 if IDNumber==70

recode cormobidity 0=1 if IDNumber==71

recode cormobidity 0=1 if IDNumber==72

recode cormobidity 0=4 if IDNumber==83

recode cormobidity 0=5 if IDNumber==89

recode cormobidity 0=1 if IDNumber==90

recode cormobidity 0=3 if IDNumber==103

recode cormobidity 0=1 if IDNumber==105

recode cormobidity 0=1 if IDNumber==106

recode cormobidity 0=1 if IDNumber==107

recode cormobidity 0=3 if IDNumber==113

recode cormobidity 0=1 if IDNumber==118

recode cormobidity 0=1 if IDNumber==119

recode cormobidity 0=1 if IDNumber==121

recode cormobidity 0=1 if IDNumber==131

recode cormobidity 0=1 if IDNumber==132

recode cormobidity 0=1 if IDNumber==133

recode cormobidity 0=1 if IDNumber==134

recode cormobidity 0=1 if IDNumber==141
```

```
recode cormobidity 0=2 if IDNumber==143

recode cormobidity 0=1 if IDNumber==146

recode cormobidity 0=1 if IDNumber==147

recode cormobidity 0=1 if IDNumber==150

recode cormobidity 0=1 if IDNumber==152

recode cormobidity 0=1 if IDNumber==159

recode cormobidity 0=1 if IDNumber==161

recode cormobidity 0=1 if IDNumber==162

recode cormobidity 0=2 if IDNumber==169


label define cormobidvals 0 "None" 1"Tuberculosis" 2"Karposis Sarcoma/Cancer" 3"
Hepatitis" 4"Meningitis" 5"Severe Anaemia"

label values cormobidity cormobidvals

label variable cormobidity "coinfection"
```

Data cleaning

*ID number 66 - envelope missing so number never allocated

drop if IDNumber==66

*Gender values restricted to 1 and 0

recode CG 2=1 if IDNumber==103

*ID number 75 correct allocation

replace A_PB="CON" if IDNumber==75

replace A_PF="CON" if IDNumber==75

*To check all patient names are the same

list IDNumber PN_PB PN_PF PN_DE if PN_PB!=PN_PF | PN_PF!=PN_DE | PN_DE!=PN_PB

*All patient names OK 12/10/13 therefore drop

drop PN_PF PN_DE

*To check all patient addresses are the same

list IDNumber Address_PB Address_PF if Address_PB!=Address_PF

*All patient addresses OK 12/10/13 therefore drop

drop Address_PF

*To check all carer names are the same

list IDNumber CN_PB CN_PF CN_DE if CN_PB!=CN_PF | CN_PF!=CN_DE | CN_DE!=CN_PB

```
*All carer names OK 12/10/13 therefore drop

drop CN_PF CN_DE


*Both source of referral variables OK 12/10/13 therefore drop

drop SOR_PF


*To check  all carer relationship to patient are the same

list IDNumber Rel_PCB Rel_CF if Rel_PCB!=Rel_CF


*Both relationships the same 12/10/13

drop Rel_CF


*Discrepancy identified and now corrected 19/10/13

replace Rel_PCB="husband-wife" if IDNumber==92


*Check allocation variables are consistent

list IDNumber A_PB A_CB A_PF A_CF if A_PB!=A_CB | A_PB!=A_PF | A_PB!=A_CF |
A_CB!=A_PF | A_CB!=A_CF | A_PF!=A_CF


*Allocation variables consistent 12/10/13

drop A_CB A_PF A_CF

encode A_PB, gen (Allocation)


*To check recruitment centre's are the same

list IDNumber SC_PCB SC_PCF if SC_PCB!=SC_PCF


*Centres same 12/10/13 at the same

drop SC_PCF
```

```
*Tidying up and encoding recruitment centre variable

encode SC_PCB, gen (SC_PCBn)

recode SC_PCBn 2=1 3=2

label define cenvals 1 "Ekwendeni" 2 "Mzuzu"

label values SC_PCBn cenvals

drop SC_PCB

rename SC_PCBn SC_PCB
```

Encoding string variables

*how to make variables based on number of missing

*egen rowmean

*egen rowmiss

*how to run lists of variables

*Understand that whenever Stata wants a varlist it can be a list of variables, such as

*list length turn

* or it can be all variables starting with a certain prefix

* list rep*

* (meaning all variables named "rep" followed by something), or it can be a range of variables

*list mpg-weight

* (meaning all variables mpg through weight in the order that the variables are recorded in the dataset).

*You can even combine all three syntaxes:

* list length turn rep* mpg-weight

*encoding pain location before

encode BPIA1_PB, gen (BPIA1_PBn)

encode BPIA2_PB, gen (BPIA2_PBn)

encode BPIA3_PB, gen (BPIA3_PBn)

encode BPIA4_PB, gen (BPIA4_PBn)

encode BPIA5_PB, gen (BPIA5_PBn)

encode BPIA6_PB, gen (BPIA6_PBn)

encode BPIA7_PB, gen (BPIA7_PBn)

encode BPIA8_PB, gen (BPIA8_PBn)

*encoding pain location after

```
  encode BPIA1_PF, gen (BPIA1_PFn)

  encode BPIA2_PF, gen (BPIA2_PFn)

  encode BPIA3_PF, gen (BPIA3_PFn)

  encode BPIA4_PF, gen (BPIA4_PFn)

  encode BPIA5_PF, gen (BPIA5_PFn)

  encode BPIA6_PF, gen (BPIA6_PFn)

  encode BPIA7_PF, gen (BPIA7_PFn)

  encode BPIA8_PF, gen (BPIA8_PFn)


  *creating binary measure for pain location before

  gen GP_PB=0

  recode GP_PB 0=1 if BPIA1_PBn==2 | BPIA1_PBn==3

  label variable GP_PB "Generalised Pain before"


  gen HN_PB=0

  recode HN_PB 0=1 if BPIA1_PBn==4 | BPIA1_PBn==5 | BPIA1_PBn==6 |
BPIA1_PBn==7 | BPIA1_PBn==8

  label variable HN_PB "Head & Neck Pain before"


  gen MS_PB=0

  recode MS_PB 0=1 if BPIA1_PBn==1 | BPIA1_PBn==9

  label variable MS_PB "Mouth sores before"


  gen LJP_PB=0

  recode LJP_PB 0=1 if BPIA2_PBn==2 | BPIA2_PBn==3 | BPIA3_PBn<5 |
BPIA6_PBn!=. | BPIA7_PBn==1 | (BPIA7_PBn>2 & BPIA7_PBn<11)

  label variable LJP_PB "Limb & Joint Pain before"
```

```
  gen CA_PB=0

  recode CA_PB 0=1 if BPIA4_PBn<7| BPIA5_PBn<3

  recode CA_PB 0=1 if
BPIA4_PBn==1|BPIA4_PBn==2|BPIA4_PBn==3|BPIA4_PBn==4|BPIA4_PBn==5|BPI
A4_PBn==6 |BPIA5_PBn==1|BPIA5_PBn==2

  label variable CA_PB "Chest & Abdominal Pain before"



  gen BP_PB=0

  recode BP_PB 0=1 if BPIA7_PBn==2|BPIA8_PBn<4

  recode BP_PB 0=1 if BPIA7_PBn==2|BPIA8_PBn==1|
BPIA8_PBn==2|BPIA8_PBn==3

  label variable BP_PB "Back pain before"



  *creating binary measure for pain location after

  gen GP_PF=0

  recode GP_PF 0=1 if BPIA1_PFn==3 | BPIA1_PFn==4 | BPIA1_PFn==6

  label variable GP_PF "Generalised Pain after"



  gen HN_PF=0

  recode HN_PF 0=1 if BPIA1_PFn==5|BPIA1_PFn==6| BPIA1_PFn==7 |
BPIA1_PFn==8

  label variable HN_PF "Head & Neck Pain after"



  gen MS_PF=0

  recode MS_PF 0=1 if BPIA1_PFn==2 | BPIA1_PBn==9

  label variable MS_PF "Mouth sores after"



  gen LJP_PF=0

  recode LJP_PF 0=1 if BPIA2_PFn==2 | BPIA2_PFn==3 | BPIA2_PFn==4 |
BPIA3_PBn!=. | BPIA6_PBn!=.| BPIA7_PBn!=.

  label variable LJP_PF "Limb & Joint Pain after"
```

```
gen CA_PF=0

recode CA_PF 0=1 if BPIA4_PBn!=.| BPIA5_PBn!=.

label variable CA_PF "Chest & Abdominal Pain after"


gen BP_PF=0

recode BP_PF 0=1 if BPIA8_PFn<4

label variable BP_PF "Back pain after"


*encoding treatment before

gen amitrip_PB=0

recode amitrip_PB 0=1 if regexm(BPIQ6_PB, "Ami")

recode amitrip_PB 0=1 if regexm(BPIQ6_PB, "ami")


gen panadol_PB=0

recode panadol_PB 0=1 if regexm(BPIQ6_PB, "Pan")

recode panadol_PB 0=1 if regexm(BPIQ6_PB, "pan")


gen Brufen_PB=0

recode Brufen_PB 0=1 if regexm(BPIQ6_PB, "Bru")

recode Brufen_PB 0=1 if regexm(BPIQ6_PB, "bru")


gen Codeine_PB=0

recode Codeine_PB 0=1 if regexm(BPIQ6_PB, "Cod")

recode Codeine_PB 0=1 if regexm(BPIQ6_PB, "cod")


gen Aspirin_PB=0

recode Aspirin_PB 0=1 if regexm(BPIQ6_PB, "Asp")
```

```
recode Aspirin_PB 0=1 if regexm(BPIQ6_PB, "asp")

gen Diclofenac_PB=0
recode Diclofenac_PB 0=1 if regexm(BPIQ6_PB, "Dic")
recode Diclofenac_PB 0=1 if regexm(BPIQ6_PB, "dic")
recode Diclofenac_PB 0=1 if regexm(BPIQ6_PB, "Dec")
recode Diclofenac_PB 0=1 if regexm(BPIQ6_PB, "dec")

gen Indocid_PB=0
recode Indocid_PB 0=1 if regexm(BPIQ6_PB, "Ind")
recode Indocid_PB 0=1 if regexm(BPIQ6_PB, "ind")

*creating a variable for medication number before
gen mednum_PB=amitrip_PB + panadol_PB + Brufen_PB + Codeine_PB +
Aspirin_PB + Diclofenac_PB + Indocid_PB

*encoding treatment after
gen amitrip_PF=0
recode amitrip_PF 0=1 if regexm(BPIQ6_PF, "Ami")
recode amitrip_PF 0=1 if regexm(BPIQ6_PF, "ami")

gen panadol_PF=0
recode panadol_PF 0=1 if regexm(BPIQ6_PF, "Pan")
recode panadol_PF 0=1 if regexm(BPIQ6_PF, "pan")

gen Brufen_PF=0
recode Brufen_PF 0=1 if regexm(BPIQ6_PF, "Bru")
recode Brufen_PF 0=1 if regexm(BPIQ6_PF, "bru")
```

```
gen Codeine_PF=0

recode Codeine_PF 0=1 if regexm(BPIQ6_PF, "Cod")

recode Codeine_PF 0=1 if regexm(BPIQ6_PF, "cod")


gen Aspirin_PF=0

recode Aspirin_PF 0=1 if regexm(BPIQ6_PF, "Asp")

recode Aspirin_PF 0=1 if regexm(BPIQ6_PF, "asp")


gen Diclofenac_PF=0

recode Diclofenac_PF 0=1 if regexm(BPIQ6_PF, "Dic")

recode Diclofenac_PF 0=1 if regexm(BPIQ6_PF, "dic")

recode Diclofenac_PF 0=1 if regexm(BPIQ6_PF, "Dec")

recode Diclofenac_PF 0=1 if regexm(BPIQ6_PF, "dec")


gen Indocid_PF=0

recode Indocid_PF 0=1 if regexm(BPIQ6_PF, "Ind")

recode Indocid_PF 0=1 if regexm(BPIQ6_PF, "ind")


gen Morphine_PF=0

recode Morphine_PF 0=1 if regexm(BPIQ6_PF, "Mor")

recode Morphine_PF 0=1 if regexm(BPIQ6_PF, "mor")


* creating a variable for medication number after

gen mednum_PF=amitrip_PF + panadol_PF + Brufen_PF + Codeine_PF +
Aspirin_PF + Diclofenac_PF + Indocid_PF + Morphine_PF


*creating a binary variable for type of medication at baseline

gen Meds_PB= mednum_PB

recode Meds_PB 0=0 1=1 2=1
```

```
label values Meds_PB medsPB

label define Meds_PB 0 "No" 1"Yes"

label var Meds_PB "Medication at baseline"


*creating a binary variable for type of medication at follow-up

gen Meds_PF=mednum_PF

recode Meds_PF 0=0 1=1 2=1 3=1

label values Meds_PF medsPF

label define Meds_PF 0 "No" 1"Yes"

label var Meds_PF "Medication as follow-up"


*creating new code for referring centre

 gen SOR_PBn=0

 recode SOR_PBn 0=1 if regexm(SOR_PB, "Ant")

 recode SOR_PBn 0=1 if regexm(SOR_PB, "HIV")

 recode SOR_PBn 0=1 if regexm(SOR_PB, "HTC")

 recode SOR_PBn 0=2 if regexm(SOR_PB, "Fem")

 recode SOR_PBn 0=2 if regexm(SOR_PB, "Ekw")

 recode SOR_PBn 0=2 if regexm(SOR_PB, "Mal")

 recode SOR_PBn 0=3 if regexm(SOR_PB, "TB")

 recode SOR_PBn 0=4 if regexm(SOR_PB, "Pal")

 recode SOR_PBn 0=4 if regexm(SOR_PB, "Wan")

 recode SOR_PBn 0=5 if regexm(SOR_PB, "Rai")

 recode SOR_PBn 0=5 if regexm(SOR_PB, "Mzu")

 label define SOR_PBn 1 "HIV testing clinic" 2"Medical wards" 3"TB ward"
4"Ekwendeni/Wanangwa clinic" 5"Mzuzu/Rainbow clinic"

 label values SOR_PBn SOR_PBn

 label variable SOR_PBn "referring centre"
```

```
 gen Ptage=(DOC_DA - DOBP_DA)/365.25

 gen Crage=(DOC_DA - DOBC_DA)/365.25

 *Time between approach and consent

 gen AppCon=DOC_DA - DOIA_DA

 *Time between consent (randomisation) and follow-up

 gen ConFup= DOFA_DA - DOC_DA if p_attrition==0


tab IDNumber if GP_PB==1|HN_PB==1| MS_PB==1|LJP_PB==1|CA_PB==1|
BP_PB==1

 bysort Allocation:tab IDNumber if GP_PB==1|HN_PB==1|
MS_PB==1|LJP_PB==1|CA_PB==1| BP_PB==1

 bysort Allocation:tab IDNumber if GP_PF==1|HN_PF==1|
MS_PF==1|LJP_PF==1|CA_PF==1| BP_PF==1
```

Transposing outcome variables

```
*patient outcomes before


*Outcome 1

*This is BPIQ4 item relating to average pain severity

*If we are to make this on a scale of 1 to 100 with 100 being better then...

generate double u = runiform()

sort u

gen PrimaryB=100-(10*BPIQ4_PB)

label variable PrimaryB "Patient BPI average pain before (O1)"

list PrimaryB BPIQ4_PB IDNumber if _n<10

drop u


*Outcome 2

*BPI 7 items relating to interference, converted to a 0 to 100 scale with higher
scores indicating less interference. Calculated for patients with no more than 2
missing items

generate double u = runiform()

sort u

egen BPImiss_PB= rowmiss (BPIQ8aPB - BPIQ8gPB)

egen BPImean_PB= rowmean (BPIQ8aPB - BPIQ8gPB) if BPImiss_PB<3

gen  BPItotal_PB= 100*((10-BPImean_PB)/10)

label variable BPItotal_PB "Patient BPI pain interference before (O2)"

list IDNumber BPImean_PB BPItotal_PB BPIQ8aPB-BPIQ8gPB if _n<10

tab BPImiss_PB

drop u


*Outcome 3
```

```
*PPQ-K 9 items relating to pain management knowledge, converted to 0 to 100, higher scores indicating greater knowledge. Calculated for patients with no more than 3 missing items.

generate double u = runiform()

sort u

egen PPQmiss_PB= rowmiss (PPQ1_PB - PPQ9_PB)

egen PPQmean_PB= rowmean (PPQ1_PB - PPQ9_PB) if PPQmiss_PB<4

gen  PPQtotal_PB= 100*((10-PPQmean_PB)/10)

label variable PPQtotal_PB "Patient pain knowledge before (O3)"

list IDNumber PPQmean_PB PPQtotal_PB PPQ1_PB-PPQ9_PB if _n<10

tab PPQmiss_PB

drop u


*Outcome 4

*POS 7 items, converted to a 0 to 100 scale with higher scores indicating better QOL. Calculated for patients with no more than 2 missing items.

generate double u = runiform()

sort u

egen POSmiss_PB = rowmiss (POSQ1_PB - POSQ7_PB)

egen POSmean_PB = rowmean (POSQ1_PB - POSQ7_PB) if POSmiss_PB<3

gen POStotal_PB = 100*((5-POSmean_PB)/5)

label variable POStotal_PB "Patient QOL before (O4)"

list POSmiss_PB POSmean_PB POStotal_PB POSQ1_PB - POSQ7_PB if _n<10

tab POSmiss_PB

drop u


*Carers outcomes before

*Outcome 5

*FPQ-K 9 items relating to carer pain management knowledge, converted to a 0 to 100 scale, higher scores indicating greater knowledge. Calculated for carers with no more than 3 missing items
```

```
generate double u = runiform()

sort u

egen FPQmiss_CB= rowmiss (FPQ1_CB - FPQ9_CB)

egen FPQmean_CB= rowmean (FPQ1_CB - FPQ9_CB) if FPQmiss_CB<4

gen  FPQtotal_CB= 100*((10-FPQmean_CB)/10)

label variable FPQtotal_CB "Carer pain knowledge before (O5)"

list FPQmean_CB FPQtotal_CB FPQ1_CB-FPQ9_CB if _n<10

tab FPQmiss_CB

drop u


*Outcome 6

*PCRS 16 items relating to carer motivation, converted to a 0 to 100 scale, with
higher scores indicating greater motivation. Calculated for carers with no more than
5 missing items

generate double u = runiform()

sort u

egen PCRSmiss_CB= rowmiss (PCRSQ1_CB - PCRSQ16_CB)

egen PCRSmean_CB= rowmean (PCRSQ1_CB - PCRSQ16_CB) if PCRSmiss_CB<6

gen  PCRStotal_CB= 100*((PCRSmean_CB)/4)

label variable PCRStotal_CB "Carer motivation before (O6)"

list PCRSmiss_CB PCRSmean_CB PCRStotal_CB PCRSQ1_CB - PCRSQ16_CB if _n<10

tab PCRSmiss_CB

drop u


*Outcome 7

*POS 3 items, converted to a 0 to 100 scale with higher scores indicating better
carer QOL. Calculated for carers with no more than 1 missing item.

generate double u = runiform()

sort u

egen POSmiss_CB = rowmiss (POSQ8_CB - POSQ10_CB)
```

```
egen POSmean_CB = rowmean (POSQ8_CB - POSQ10_CB) if POSmiss_CB<2

gen POStotal_CB = 100*((5-POSmean_CB)/5)

label variable POStotal_CB "Carer QOL before (O7)"

list POSmiss_CB POSmean_CB POStotal_CB POSQ8_CB - POSQ10_CB if _n<10

tab POSmiss_CB

drop u


*Patient outcomes after

*Outcome 1

generate double u = runiform()

sort u

gen FollowupB=100-(10*BPIQ4_PF)

label variable FollowupB "Patient BPI average pain after (O1)"

list FollowupB BPIQ4_PF IDNumber if _n<10

drop u


*Outcome 2

*BPI 7 items relating to interference, converted to a 0 to 100 scale with higher
scores indicating less interference. Calculated for patients with no more than 2
missing items

generate double u = runiform()

sort u

egen BPImiss_PF= rowmiss (BPIQ8a_PF - BPIQ8g_PF)

egen BPImean_PF= rowmean (BPIQ8a_PF - BPIQ8g_PF) if BPImiss_PF<3

gen  BPItotal_PF= 100*((10-BPImean_PF)/10)

label variable BPItotal_PF "Patient BPI pain interference after (O2)"

list IDNumber BPImean_PF BPItotal_PF BPIQ8a_PF-BPIQ8g_PF if _n<10

tab BPImiss_PF

drop u
```

```
*Outcome 3

*PPQ-K 9 items relating to pain management knowledge, converted to 0 to 100,
higher scores indicating greater knowledge. Calculated for patients with no more
than 3 missing items.

generate double u = runiform()

sort u

egen PPQmiss_PF= rowmiss (PPQ1_PF - PPQ9_PF)

egen PPQmean_PF= rowmean (PPQ1_PF - PPQ9_PF) if PPQmiss_PF<4

gen  PPQtotal_PF= 100*((10-PPQmean_PF)/10)

label variable PPQtotal_PF "Patient pain knowledge after (O3)"

list IDNumber PPQmean_PF PPQtotal_PF PPQ1_PF-PPQ9_PF if _n<10

tab PPQmiss_PF

drop u


*Outcome 4

*POS 7 items, converted to a 0 to 100 scale with higher scores indicating better QOL.
Calculated for patients with no more than 2 missing items.

generate double u = runiform()

sort u

egen POSmiss_PF = rowmiss (POSQ1_PF - POSQ7_PF)

egen POSmean_PF = rowmean (POSQ1_PF - POSQ7_PF) if POSmiss_PF<3

gen POStotal_PF = 100*((5-POSmean_PF)/5)

label variable POStotal_PF "Patient QOL after (O4)"

list IDNumber POSmiss_PF POSmean_PF POStotal_PF POSQ1_PF - POSQ7_PF if
_n<10

tab POSmiss_PF

drop u


*Carers outcomes after
```

```
*Outcome 5

*FPQ-K 9 items relating to carer pain management knowledge, converted to a 0 to 100 scale, higher scores indicating greater knowledge. Calculated for carers with no more than 3 missing items

generate double u = runiform()

sort u

egen FPQmiss_CF= rowmiss (FPQ1_CF - FPQ9_CF)

egen FPQmean_CF= rowmean (FPQ1_CF - FPQ9_CF) if FPQmiss_CF<4

gen  FPQtotal_CF= 100*((10-FPQmean_CF)/10)

label variable FPQtotal_CF "Carer pain knowledge after (O5)"

list IDNumber FPQmean_CF FPQtotal_CF FPQ1_CF-FPQ9_CF if _n<10

tab FPQmiss_CF

drop u


*Outcome 6

*PCRS 16 items relating to carer motivation, converted to a 0 to 100 scale, with higher scores indicating greater motivation. Calculated for carers with no more than 5 missing items

generate double u = runiform()

sort u

egen PCRSmiss_CF= rowmiss (PCRSQ1_CF - PCRSQ16_CF)

egen PCRSmean_CF= rowmean (PCRSQ1_CF - PCRSQ16_CF) if PCRSmiss_CF<6

gen  PCRStotal_CF= 100*((PCRSmean_CF)/4)

label variable PCRStotal_CF "Carer motivation after (O6)"

list IDNumber PCRSmiss_CF PCRSmean_CF PCRStotal_CF PCRSQ1_CF - PCRSQ16_CF if _n<10

tab PCRSmiss_CF

drop u


*Outcome 7
```

```
*POS 3 items, converted to a 0 to 100 scale with higher scores indicating better carer QOL. Calculated for carers with no more than 1 missing item.

generate double u = runiform()

sort u

egen POSmiss_CF = rowmiss (POSQ8_CF - POSQ10_CF)

egen POSmean_CF = rowmean (POSQ8_CF - POSQ10_CF) if POSmiss_CF<2

gen POStotal_CF = 100*((5-POSmean_CF)/5)

label variable POStotal_CF "Carer QOL after (O7)"

list IDNumber POSmiss_CF POSmean_CF POStotal_CF POSQ8_CF - POSQ10_CF if _n<10

tab POSmiss_CF

drop u


**** Create change scores for seven outcomes

*Outcome 1

gen change1 = FollowupB - PrimaryB


*Outcome 2

gen change2 = BPItotal_PF - BPItotal_PB


*Outcome 3

 gen change3 = PPQtotal_PF - PPQtotal_PB


*Outcome 4

gen change4 = POStotal_PF - POStotal_PB


*Outcome 5

gen change5 = FPQtotal_CF - FPQtotal_CB
```

```
*Outcome6

gen change6 = PCRStotal_CF - PCRStotal_CB


*Outcome7

gen change7 = POStotal_CF - POStotal_CB
```

Ordering new variables (patient/carer baseline/follow-up)

order IDNumber Allocation SC_PCB DOBP_DA DOBC_DA DOIA_DA DOC_DA DOFS_DA DOFA_DA RELCOLL PN_PB Address_PB CN_PB SOR_PB SOR_PBn Rel_PCB A_PB > PMARCOLL CMARCOLL POCCOLL COCOLL PG_DE CG_DE REL_DE PE_DE CE_DE PR_DE CR_DE PO_DE CO_DE DOP_DA PN_PB Address_PB CN_PB SOR_PB Rel_PCB A_PB B> PIA1_PB BPIA2_PB BPIA3_PB BPIA4_PB BPIA5_PB BPIA6_PB BPIA7_PB BPIA8_PB BPIA1_PBn BPIA2_PBn BPIA3_PBn BPIA4_PBn BPIA5_PBn BPIA6_PBn BPIA7_PB> n BPIA8_PBn GP_PB HN_PB MS_PB LJP_PB CA_PB BP_PB BPIQ2_PB BPIQ3_PB BPIQ4_PB BPIQ5_PB BPIQ6_PB amitrip_PB panadol_PB Brufen_PB Codeine_PB Aspirin_PB Diclofenac_PB Indocid_PB BPIQ7_PB BPIQ8aPB BPIQ8bPB BPIQ8cPB BPIQ8dPB BPIQ8ePB BPIQ8fPB BPIQ8gPB PPQ1_PB PPQ2_PB PPQ3_PB PPQ4_PB P> PQ5_PB PPQ6_PB PPQ7_PB PPQ8_PB PPQ9_PB PPQ10_PB PPQ11_PB PPQ12_PB PPQ13_PB PPQ14_PB PPQ15_PB PPQ16_PB POSQ1_PB POSQ2_PB POSQ3_PB POSQ4_PB P> OSQ5_PB POSQ6_PB POSQ7_PB FPQ1_CB FPQ2_CB FPQ3_CB FPQ4_CB FPQ5_CB FPQ6_CB FPQ7_CB FPQ8_CB FPQ9_CB FPQ10_CB FPQ11_CB FPQ12_CB FPQ13_CB FPQ14> _CB FPQ15_CB FPQ16_CB PCRSQ1_CB PCRSQ2_CB PCRSQ3_CB PCRSQ4_CB PCRSQ5_CB PCRSQ6_CB PCRSQ7_CB PCRSQ8_CB PCRSQ9_CB PCRSQ10_CB PCRSQ11_CB PCRSQ> 12_CB PCRSQ13_CB PCRSQ14_CB PCRSQ15_CB PCRSQ16_CB POSQ8_CB POSQ9_CB POSQ10_CB BPIA1_PF BPIA2_PF BPIA3_PF BPIA4_PF BPIA5_PF BPIA6_PF BPIA7_P> F BPIA8_PF BPIA1_PFn BPIA2_PFn BPIA3_PFn BPIA4_PFn BPIA5_PFn BPIA6_PFn BPIA7_PFn BPIA8_PFn GP_PF HN_PF MS_PF LJP_PF CA_PF BP_PF BPIQ2_PF BP> IQ3_PF BPIQ4_PF BPIQ5_PF BPIQ6_PF amitrip_PF panadol_PF Brufen_PF Codeine_PF Aspirin_PF Diclofenac_PF Indocid_PF Morphine_PF BPIQ7_PF BPIQ8> a_PF BPIQ8b_PF BPIQ8c_PF BPIQ8d_PF BPIQ8e_PF BPIQ8f_PF BPIQ8g_PF PPQ1_PF PPQ2_PF PPQ3_PF PPQ4_PF PPQ5_PF PPQ6_PF PPQ7_PF PPQ8_PF PPQ9_PF PP> Q10_PF PPQ11_PF PPQ12_PF PPQ13_PF PPQ14_PF PPQ15_PF PPQ16_PF POSQ1_PF POSQ2_PF POSQ3_PF POSQ4_PF POSQ5_PF POSQ6_PF POSQ7_PF FPQ1_CF FPQ2_CF> FPQ3_CF FPQ4_CF FPQ5_CF FPQ6_CF FPQ7_CF FPQ8_CF FPQ9_CF FPQ10_CF FPQ11_CF FPQ12_CF FPQ13_CF FPQ14_CF FPQ15_CF FPQ16_CF PCRSQ1_CF PCRSQ2_CF> PCRSQ3_CF PCRSQ4_CF PCRSQ5_CF PCRSQ6_CF PCRSQ7_CF PCRSQ8_CF PCRSQ9_CF PCRSQ10_CF, first.

Producing output for baseline tables and figures

```
tab Allocation

tab c_attrition if Allocation==2 & p_attrition==0 & c_attrition!=0

tab p_attrition if Allocation==2 & p_attrition!=0 & c_attrition!=0


tab c_attrition if Allocation==1 & p_attrition==0 & c_attrition!=0

tab p_attrition if Allocation==1 & p_attrition!=0 & c_attrition!=0


*Table 1 Groups at baseline (patients)

bysort Allocation: summ Ptage

bysort Allocation: tab PG_DE

bysort Allocation: tab PMARCOLL

bysort Allocation: tab PE_DE

bysort Allocation: tab PR_DE

bysort Allocation: tab POCCOLL

bysort Allocation: summ PrimaryB

bysort Allocation: summ BPItotal_PB

bysort Allocation: summ PPQtotal_PB

bysort Allocation: summ POStotal_PB


bysort Allocation:tab Meds_PB

bysort Allocation:tab Meds_PF


bysort Allocation:tab GP_PB

bysort Allocation:tab HN_PB

bysort Allocation:tab MS_PB

bysort Allocation:tab LJP_PB
```

```
bysort Allocation:tab CA_PB

bysort Allocation:tab BP_PB


bysort Allocation:tab GP_PF

bysort Allocation:tab HN_PF

bysort Allocation:tab MS_PF

bysort Allocation:tab LJP_PF

bysort Allocation:tab CA_PF

bysort Allocation:tab BP_PF


*Table 1 Groups at baseline (carers)

bysort Allocation: summ Crage

bysort Allocation: tab CG_DE

bysort Allocation: tab CMARCOLL

bysort Allocation: tab CE_DE

bysort Allocation: tab CR_DE

bysort Allocation: tab COCOLL

bysort Allocation: tab RELCOLL

bysort Allocation: summ FPQtotal_CB

bysort Allocation: summ PCRStotal_CB

bysort Allocation: summ POStotal_CB


*Table 1 Groups at baseline (patients and carers)

bysort Allocation: tab SOR_PBn

bysort Allocation: tab SC_PCB


bysort Allocation: summ FollowupB

bysort Allocation: summ BPItotal_PF
```

```
bysort Allocation: summ PPQtotal_PF

bysort Allocation: summ POStotal_PF


bysort Allocation: summ FPQtotal_CF

bysort Allocation: summ PCRStotal_CF

bysort Allocation: summ POStotal_CF


*means

bysort Allocation: summ change1 - change7
```

Analysis of outcomes

*patient unadjusted analyses

regress FollowupB PrimaryB Allocation SC_PCB

regress BPItotal_PF BPItotal_PB Allocation SC_PCB

regress PPQtotal_PF PPQtotal_PB Allocation SC_PCB

regress POStotal_PF POStotal_PB Allocation SC_PCB

*carers unadjusted analyses

regress FPQtotal_CF FPQtotal_CB Allocation SC_PCB

regress PCRStotal_CF PCRStotal_CB Allocation SC_PCB

regress POStotal_CF POStotal_CB Allocation SC_PCB

*adjusted analysis, as above but include age, gender, total number of pain meds

*Patient analyses

regress FollowupB PrimaryB Allocation SC_PCB Ptage PG_DE mednum_PB

regress BPItotal_PF BPItotal_PB Allocation SC_PCB Ptage PG_DE mednum_PB

regress PPQtotal_PF PPQtotal_PB Allocation SC_PCB Ptage PG_DE mednum_PB

regress POStotal_PF POStotal_PB Allocation SC_PCB Ptage PG_DE mednum_PB

*Carers analyses

regress FPQtotal_CF FPQtotal_CB Allocation SC_PCB Crage CG_DE

regress PCRStotal_CF PCRStotal_CB Allocation SC_PCB Crage CG_DE

regress POStotal_CF POStotal_CB Allocation SC_PCB Crage CG_DE

*model for medication for number of medication

```
regress mednum_PF mednum_PB Allocation SC_PCB

regress mednum_PF mednum_PB Allocation SC_PCB Ptage PG_DE


logistic Meds_PF Meds_PB Allocation SC_PCB

logistic Meds_PF Meds_PB Allocation SC_PCB Ptage PG_DE


*model for type of medication adjusted for Allocation,centre, age and gender

logistic amitrip_PF amitrip_PB Allocation SC_PCB Ptage PG_DE

logistic panadol_PF panadol_PB Allocation SC_PCB Ptage PG_DE

logistic Brufen_PF  Brufen_PB Allocation SC_PCB  Ptage PG_DE

logistic Codeine_PF Codeine_PB Allocation SC_PCB Ptage PG_DE

logistic Diclofenac_PF Diclofenac_PB Allocation SC_PCB Ptage PG_DE

logistic Aspirin_PF Aspirin_PB Allocation SC_PCB Ptage PG_DE

logistic Indocid_PF Indocid_PB Allocation SC_PCB Ptage PG_DE


logistic HN_PF HN_PB Allocation SC_PCB Ptage PG_DE

logistic MS_PF MS_PB Allocation SC_PCB Ptage PG_DE

logistic LJP_PF LJP_PB Allocation SC_PCB Ptage PG_DE

logistic BP_PF BP_PB Allocation SC_PCB Ptage PG_DE

logistic GP_PF GP_PB Allocation SC_PCB Ptage PG_DE

logistic CA_PF CA_PB Allocation SC_PCB Ptage PG_DE
```

Sensitivity analysis and checking model assumptions

recode Group 1=0 2=1

/*

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(Sensitivity analysis for Kennedy trial 1) list listopt(sepby(delta)): reg FollowupB PrimaryB Group SC_PCB

xi: rctmiss, sens(Allocation) pmmdelta(-10/0): reg FollowupB PrimaryB Allocation SC_PCB

xi: rctmiss, pmmdelta(-5): reg FollowupB PrimaryB Allocation SC_PCB

*/

label define randvals 0 "Usual care" 1 "Pain education", replace

label values Group randvals

/*

label variable c_attrition "carer attrition"

*/

*unadjusted analysis (replace square brackets with variable names)

/*

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(BPI-PS) list listopt(sepby(delta)):regress FollowupB PrimaryB Group SC_PCB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(BPI-PI) list listopt(sepby(delta)):regress BPItotal_PF BPItotal_PB Group SC_PCB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(PPK-Q) list listopt(sepby(delta)):regress PPQtotal_PF PPQtotal_PB Group SC_PCB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(APCA African POS) list listopt(sepby(delta)):regress POStotal_PF POStotal_PB Group SC_PCB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(FPQ-PK) list listopt(sepby(delta)):regress FPQtotal_CF FPQtotal_CB Group SC_PCB

```
xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05)
title(PCRS) list listopt(sepby(delta)):regress PCRStotal_CF PCRStotal_CB Group
SC_PCB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(APCA
African POS) list listopt(sepby(delta)):regress POStotal_CF POStotal_CB Group
SC_PCB

*/



*adjusted analysis, as above but include age, gender, total number of pain meds



xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(BPI-
PS) list listopt(sepby(delta)):regress FollowupB PrimaryB Group SC_PCB Ptage
PG_DE  mednum_PB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(BPI-
PI) list listopt(sepby(delta)):regress BPItotal_PF BPItotal_PB Group SC_PCB Ptage
PG_DE  mednum_PB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(PPK-
Q) list listopt(sepby(delta)):regress PPQtotal_PF PPQtotal_PB Group SC_PCB Ptage
PG_DE  mednum_PB

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(APCA
African POS-Patients) list listopt(sepby(delta)):regress POStotal_PF POStotal_PB
Group SC_PCB Ptage PG_DE  mednum_PB



xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(FPQ-
K) list listopt(sepby(delta)):regress FPQtotal_CF FPQtotal_CB Group SC_PCB Crage
CG_DE

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05)
title(PCRS) list listopt(sepby(delta)):regress PCRStotal_CF PCRStotal_CB Group
SC_PCB Crage CG_DE

xi: rctmiss, sens(Group) pmmdelta(-50/50) legend(rows(3)) stagger(0.05) title(APCA

African POS-Carers) list listopt(sepby(delta)):regress POStotal_CF POStotal_CB

Group SC_PCB Crag
```

Appendix 16 Publications

TRIALS

STUDY PROTOCOL Open Access

An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: study protocol for a randomised controlled trial

Kennedy Nkhoma[1], Jane Seymour[1*] and Antony Arthur[2]

Abstract

Background: Many HIV/AIDS patients experience pain often due to advanced HIV/AIDS infection and side effects of treatment. In sub-Saharan Africa, pain management for people with HIV/AIDS is suboptimal. With survival extended as a direct consequence of improved access to antiretroviral therapy, the prevalence of HIV/AIDS related pain is increasing. As most care is provided at home, the management of pain requires patient and family involvement. Pain education is an important aspect in the management of pain in HIV/AIDS patients. Studies of the effectiveness of pain education interventions for people with HIV/AIDS have been conducted almost exclusively in western countries.

Methods/design: A randomised controlled trial is being conducted at the HIV and palliative care clinics of two public hospitals in Malawi. To be eligible, patient participants must have a diagnosis of HIV/AIDS (stage III or IV). Carer participants must be the individual most involved in the patient's unpaid care. Eligible participants are randomised to either: (1) a 30-minute face-to-face educational intervention covering pain assessment and management, augmented by a leaflet and follow-up telephone call at two weeks; or (2) usual care. Those allocated to the usual care group receive the educational intervention after follow-up assessments have been conducted (wait-list control group). The primary outcome is pain severity measured by the Brief Pain Inventory. Secondary outcomes are pain interference, patient knowledge of pain management, patient quality of life, carer knowledge of pain management, caregiver motivation and carer quality of life. Follow-up assessments are conducted eight weeks after randomisation by palliative care nurses blind to allocation.

Discussion: This randomised controlled trial conducted in sub-Saharan Africa among people living with HIV/AIDS and their carers will assess whether a pain education intervention is effective in reducing pain and improving pain management, quality of life and carer motivation.

Trial registration: Current Controlled Trials ISRCTN72861423.

Keywords: HIV/AIDS, Trial, Pain, Carers, Educational intervention, Palliative care

* Correspondence: jane.seymour@nottingham.ac.uk
[1]Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care, School of Nursing, Midwifery and Physiotherapy, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, UK
Full list of author information is available at the end of the article

Background

It is estimated that 34 million people were living with HIV/AIDS at the end of 2010 [1]. In 2010, there were 1.8 million deaths from AIDS, and 2.7 million people newly infected globally. In the same year, 1.4 million people commenced HIV medication, an increase of 27% in the number of people receiving treatment from the previous year. Greater access to effective treatment has led to a 19% decline in deaths among people living with HIV/AIDS between 2004 and 2009.

Sub-Saharan Africa has 10% of the world's population, but it is home to 67% of all people living with HIV/AIDS, making it the region worst-affected by HIV/AIDS [1,2]. Antiretroviral therapy can dramatically increase survival and years of healthy life, but is unavailable in some parts of the region [2]. In 2009 in sub-Saharan Africa, 37% of the population eligible for HIV medication were treated, compared with 2% seven years earlier [3].

In Malawi the prevalence of HIV/AIDS is estimated at 11% of the population aged between 15 and 49 years, with around 920,000 people living with HIV/AIDS at the end of 2010 [1,2]. Approximately 250 people are newly infected each day, and at least 70% of Malawi's hospital beds are occupied by HIV/AIDS patients, making Malawi the 12th worst-affected country with HIV/AIDS worldwide [4]. Substantial progress has been made in the provision of HIV medication. By the end of 2010, an estimated 250,000 people had commenced HIV treatment representing 52% of those in need [1]. However, due to inequities within Malawi's health system, access to HIV medication is suboptimal [5-8]. One initiative to help deal with the challenge of accessing HIV medication has been the involvement of nurses in the prescription and administration of medications. Trained health assistants now provide HIV counselling services to patients, and this has resulted in a greater proportion of patients starting HIV medication within three weeks of diagnosis [1].

Advanced HIV disease infection and its treatment with HIV medication are associated with physical and psychological symptoms. These require focused assessment and management using locally available resources and interventions to optimise quality of life for patients and their carers [9]. The negative impact of pain on quality of life has been documented in many studies [10,11]. Pain is a major problem for people living with HIV/AIDS [12-14]. Pain is the most frequent and main cause of psychological distress [15,16]. Experiencing pain can reduce adherence to drugs and quality of life for HIV/AIDS patients [17-21].

Inadequate pain control remains a challenge for HIV/AIDS patients and has an impact on their quality of life [19,20]. Pain is experienced throughout the disease trajectory, severity being associated with later World Health Organisation (WHO) clinical stage, [22-24] with an estimated 80% of people with advanced HIV infection experiencing severe pain [25]. Pain is also experienced due to the effects of HIV medication [26,27]. With advances being made in improving access to HIV drugs in resource poor countries, HIV patients are living longer, and, therefore, experiencing pain over a longer period [28,29]. For cost-related reasons there is rarely the opportunity for second-line antiretroviral medication to be prescribed when first-line antiretroviral therapy is poorly tolerated [30]. There is a need to provide effective interventions to HIV/AIDS patients in alleviating and managing pain. Previous trials conducted in western countries of interventions to improve medication adherence have produced conflicting results; one found evidence that medication adherence and knowledge can be improved [31] and another suggested that quality of life outcomes were worse in the intervention group [32]. In a trial of a symptom management manual for people with HIV/AIDS, symptom frequency was reduced but only a small number of trial centres were in sub-Saharan Africa [9]. The majority of centres were in the United States where the healthcare context is very different. None of these trials directly involved unpaid carers, a group likely to play a key role in the management of pain of those for whom they care.

Aim

The aim of this trial is to evaluate the effect of an educational intervention for patients with HIV/AIDS and their carers. The study will test the following hypotheses:

1. Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will report less severity of pain.
2. Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will report less interference of pain in their daily activities.
3. Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will have a greater knowledge of pain management.
4. Compared with usual care, patients with HIV/AIDS who receive a pain education intervention will have a better quality of life.
5. Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have greater knowledge of pain management.
6. Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have greater motivation to provide care.

7. Compared with usual care, carers of patients with HIV/AIDS who receive the pain education intervention will have a better quality of life.

Methods/design

Overview of study design

The study is a two-centre randomised wait-list controlled trial. Participants (patients with HIV/AIDS and their carers) randomly allocated to a pain education intervention group receive a leaflet-based educational intervention and verbal instructions for approximately 30 minutes on pain assessment and management in addition to usual care. Participants randomly allocated to the usual care group receive standard care, but receive the leaflet-based educational intervention on completion of follow-up measures for both treatment groups (wait-list control). Participants are assessed at baseline after providing informed consent and then randomly allocated to either the pain education intervention or usual care arm of the trial. Follow-up assessments are conducted after eight weeks.

Setting

The trial setting is that of HIV and palliative care clinics within two public hospitals in northern Malawi. Both hospitals (Ekwendeni and Mzuzu Central) provide in-patient, clinic-based and home-based care for people with HIV/AIDS that includes active treatment and palliative care. Ekwendeni Hospital provides services funded by the government. It was one of the first hospitals in Malawi to provide free HIV/AIDS medication. Mzuzu Central Hospital is government-funded and the largest referral hospital in north Malawi for people with HIV/AIDS. The population served by these hospitals includes people from both rural and urban areas.

Study participants

Participants are people living with HIV/AIDS and their carers. All participants need to be able to read and write in English or Tumbuka (the vernacular language used in the northern part of Malawi). They must be adults aged 18 years or over.

Inclusion criteria for people living with HIV/AIDS

To be eligible for the trial, participants must have received a diagnosis of HIV/AIDS. Participants with other conditions, such as cancer and tuberculosis, are included if these conditions present alongside a diagnosis of HIV/AIDS. Eligible participants with HIV/AIDS must be at WHO clinical stages III or IV of HIV/AIDS, or with a CD4 cell count of less than 350 cells, when the presence of pain and other symptoms are more likely due to opportunistic infections or side effects of HIV treatment. Staging for trial eligibility is assessed from the medical records if recorded or through assessment by clinic staff if this information is not available.

Inclusion criteria for carers

To be eligible for inclusion, carers must be living with the person with HIV/AIDS and be identified as the individual most involved in their care.

Exclusion criteria for people living with HIV/AIDS

People living with HIV/AIDS will be excluded if they have health problems that may hinder cognition and communication, such as HIV-associated dementia. This is assessed by the attending clinical officer during history-taking at the initial assessment or at clinic review.

Recruitment

People living with HIV/AIDS in Malawi typically visit the hospital (palliative care clinics and HIV clinics) with their family members. Posters about the study entitled 'Pain Education Study' are prominently displayed and potential participants have the opportunity to be given further information about the study directly from KN or from clinic staff.

The study is introduced either during the first appointment at the HIV clinic for newly registered patients or during routine appointments at the HIV clinics or palliative care clinics for those who are already receiving HIV medication (see Figure 1). KN or the staff in these clinics inform patients about the study and provide them with information sheets. Potential participants are encouraged by KN or the clinic staff to discuss with family members before making a decision to take part.

Potential participants have between two and four weeks to consider taking part in the study. During their next appointment those who are interested in taking part in the study are asked to provide written informed consent by KN. A checklist is administered to confirm that all criteria for study eligibility are met.

Randomisation

After baseline assessments, participants are randomly allocated to the pain education intervention group or usual care group. Randomisation is implemented by KN using opaque, sealed and numbered envelopes. The envelope is opened in the presence of the participants after baseline assessments. Participants have a 50% chance of being allocated to either the pain education intervention group or usual care group. In order to limit imbalance between the treatment groups, participants are randomly assigned with block randomisation using the 'ralloc' command in Stata version 12 [33] Name of manufacturer: StataCorp, College Station, Texas, USA. Randomisation is stratified by the

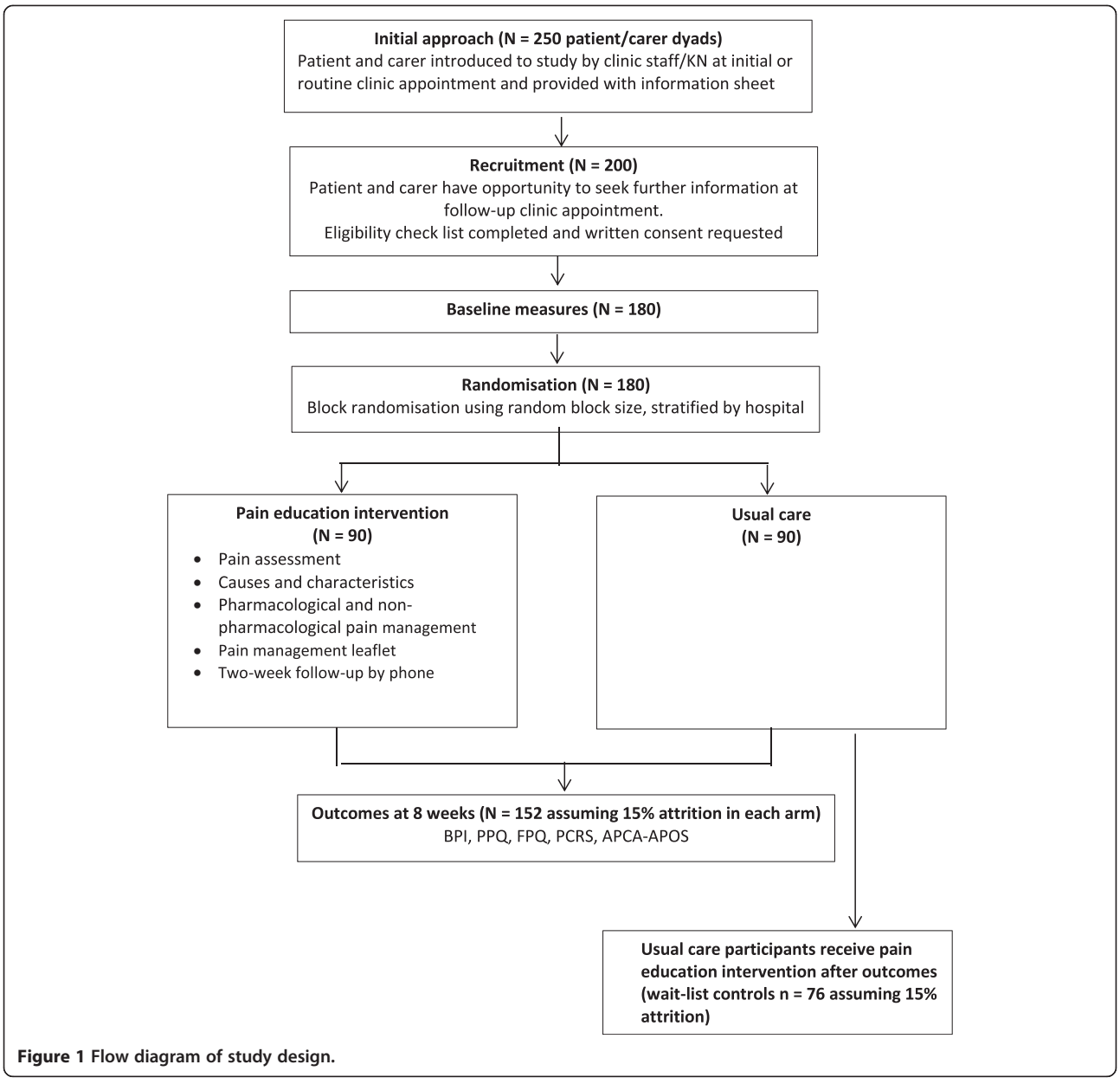


Figure 1 Flow diagram of study design.

recruiting hospital. KN is not involved in the preparation of the envelopes and is blind to block size.

Interventions

Usual care

Assistance with pain management for patients with HIV/AIDS is currently provided by hospital-based palliative care nurses and typically delivered in either a palliative care clinic or HIV clinic. Information relating to pain medication is typically responsive rather than proactive and *ad hoc* rather than systematic. Information is provided when requested by patients or carers. The focus is mostly restricted to pharmacological treatment of pain. Pain assessments are not usually conducted in a systematic way and not recorded routinely. It is unusual for this information to be shared with patients and/or their carers.

Pain education intervention

The pain education intervention is informed by a biopsychosocial approach [34] to management of pain among people with HIV/AIDS. This conceptual framework has guided the development of the intervention in targeting adequate and effective use of analgesia (biological), providing support and knowledge to minimise distress associated with poorly controlled pain (psychological), and targeting the intervention at the level of the patient/carer dyad (social). The

intervention consists of a leaflet and health education session delivered face-to-face by KN to the participants at the HIV clinic or palliative care clinic. The face-to-face session takes approximately 30 minutes wherein KN explains the intervention to the patient and carer and both are given a copy of the leaflet and allowed to browse through it briefly. KN then discusses the contents of the leaflet with the participants and they are both encouraged to ask questions. After two weeks, participants receive a phone call reminder to enquire whether they have any further questions after reading the leaflet. The details of the session are reported in Table 1.

Measures

Baseline

After recruitment and obtaining written consent from participants, but prior to randomisation, baseline assessments are conducted by KN. Baseline assessments include relevant details from medical notes (date of diagnosis, current treatments) and demographics. Other measures taken at baseline are those used as outcomes for the trial.

The primary outcome is pain severity measured using the Brief Pain Inventory [35]. A range of secondary outcomes have been chosen due to the complex nature of the intervention. The time point between delivery of the intervention and follow-up assessments was chosen to be consistent with other studies of pain education [36,37]. Patients are assessed in terms of pain severity, pain interference with daily activities, knowledge of pain management, and quality of life. Carers are assessed in terms of knowledge of pain management, caregiver motivation and quality of life. These are measured as follows:

1. Pain severity is measured using the single item of the Brief Pain Inventory (BPI-PS) [35] where patients are asked to rate the severity of their pain on average over the last week. A rating is made on a 0 to 10 point scale with higher scores indicating greater severity of pain. This is consistent with the

Table 1 Components of the pain education intervention

Topics to be covered	Content
Introductions	Participants (patient and carer) welcomed
	Introductions and clarifications as required
	Leaflet provided and participants given time to read through
Overview of pain in HIV/AIDS	Pain defined in relation to HIV/AIDS
	Possible causes of pain in HIV/AIDS discussed
	Characteristics of pain relating to HIV/AIDS
Beliefs and myths about pain in HIV/AIDS	Participants given opportunity to share beliefs about pain in relation to HIV/AIDS
	Where appropriate misconceptions dispelled
Beliefs and myths about pain medication	Ask the participants' beliefs about use of pain medication
	Summarise and dispel misconceptions as required about pain medication
Assessment of pain in HIV/AIDS	Demonstrate with the help of body diagrams how to locate and describe pain
	Demonstrate use of pain assessment tools to rate and record pain
	Demonstrate with pain diagrams how to classify pain
	Explore type of pain experienced and strategies used to manage pain
	Discuss ways in which pain may be managed more effectively
Pharmacological management of pain	Demonstrate, using the WHO analgesic ladder, how pain is managed with medications
	Give examples of available drugs used on the WHO ladder
	Discuss most effective timing of pain medication
Non-pharmacological management of pain	Identify what non-pharmacological interventions participants are aware of and use
	Practical demonstrations on use of non-pharmacological interventions as appropriate
Other items to be covered	Participants given further opportunity to clarify any of the points discussed
	Participants encouraged to re-read the leaflet after the end of the face-to-face meeting and refer to it whenever the patient experiences pain
	Advise participants to ask for clarification about the leaflet and its contents by sending a missed call to KN who will then return the call
	Routine follow-up call at two weeks

measurement of pain severity in a number of clinical trials [38]. The BPI has been used with patients with cancer and other chronic illnesses such as HIV/AIDS [15,39] and to study the management of pain in South Africa [40].

2. Pain interference with daily activities is measured using the mean score of the seven pain interference items of the Brief Pain Inventory (BPI-PI). These items measure, on a scale of 0 to 10, the degree to which the patient reports pain interfering with each of seven activities (general activity, walking, work, mood, enjoyment of life, relations with others and sleep) and is the recommended method of assessment of pain-related functional impairment in clinical trials [41].
3. For patients, knowledge of pain management is measured using the knowledge subscale of the Patient Pain Questionnaire (PPQ-K) [42]. The PPQ-K is made up of nine items asking the patient to disagree or agree with statements about the effectiveness, timing of pain medication dosage, and adequacy of pain medication dosage. Agreement/disagreement is rated on a scale of 0 to 10. Scores range from 0 to 90 with higher scores indicating greater patient knowledge of pain management.
4. For patients, quality of life is measured using the APCA African POS [43]. The APCA African POS consists of seven items directed at patients addressing pain and symptom assessment, psychological and emotional concerns. Possible scores range from 0 to 35 with higher scores indicating worse outcomes/quality of life. The tool has been developed and tested in three African countries [44].
5. For carers, knowledge of pain management is measured using the knowledge subscale of the Family Pain Questionnaire (FPQ-K) [45]. Like the PPQ-K, the FPQ-K is made up of nine items asking the carer to disagree or agree with statements about the effectiveness, timing of pain medication dosage, and adequacy of pain medication dosage. Agreement/disagreement is rated on a scale of 0 to 10. Scores range from 0 to 90 with higher scores indicating greater carer knowledge of pain management.
6. Carer motivation is measured using the Picot Caregiver Rewards Scale (PCRS) [46]. The PCRS is a 16-item scale measuring the positive consequences of caregiving. Respondents rate the degree to which items describe positive consequences of their caregiving on a 5-point Likert scale. Possible scores range from 0 to 64 with higher scores indicating more positive caregiving experience.
7. For carers, quality of life is measured using the APCA African POS [43]. The APCA African POS consists of three items directed at carers addressing the adequacy of information the family has received, confidence in caring, and level of worry. Possible scores range from 0 to 15 with higher scores indicating worse outcomes/quality of life.

While the BPI [40] and APCA African POS [43] have both been used previously in Sub-Saharan African Populations, use of the PPQ, FPQ and PCRS has been restricted to populations in western countries. Our experience immediately prior to trial recruitment of piloting these scales as part of the questionnaires among 10 patients and 10 carers suggests that they are acceptable to and understood by members of the population of patients and carers from which our sample is being recruited.

Follow-up

Follow-up measures are conducted after eight weeks following delivery of the intervention. Nurses blind to treatment group conduct the follow-up assessments. This is implemented during the routine appointments to the HIV or palliative care clinic.

Sample size

We wish to be able to detect a mean difference of 10% between the treatment groups in the primary outcome measure (average pain severity in the BPI). A 10% improvement is the lower limit of changes considered clinically important [47]. Using a *P*-value cut-off of 0.05 to determine a statistically significant result, 76 people per arm of the trial will be needed to complete the study to give 80% power to detect such a difference. This is based on a review [48] that suggests that education-based interventions are able to produce this level of improvement in pain reduction, and that a standard deviation of 2.2 points is a liberal estimate of variability. To allow for 15% attrition, we will attempt to recruit 180 participants to the trial.

Statistical analysis

We will provide a descriptive account of the two treatment groups at baseline in terms of demographics, recruiting centre, stage of HIV/AIDS and baseline values of all study outcomes. All patients and carers will be analysed according to the group to which they were randomised. Treatment groups will be compared in terms of our primary outcome measure (pain severity using the BPI-PS treated as a continuous measure) using a linear regression model with baseline BPI and treatment group and recruiting centre as covariates. Analysis of each of the six secondary outcomes (BPI-PI, PPQ-K, APCA African POS patient score, FPQ-K, PCRS, APCA African POS carer score) will be conducted using six equivalent models with estimates of treatment effect

conditional on the value of the outcome at baseline. Sensitivity analysis will be reported and performed as follows: we will conduct secondary analyses that (1) adjust for variables that are potential predictors of outcome (for example, age, gender, stage of HIV/AIDS, medication use at baseline) and (2) make worst-case and best-case scenario assumptions about participants lost to follow-up using the Stata command 'rctmiss' [49]. Analysis will be conducted using Stata version 12 [33].

Ethical approval

The study has been approved by the University of Nottingham Medical School Research Ethics Committee (SNMP 11042012) and National Health Sciences Research Committee of Malawi (NHSRC 1023).

Discussion

Findings from this trial will inform the management of pain experienced by people living with HIV/AIDS. Previous trials of interventions designed to enhance self-management for people living with HIV/AIDS have been conducted either exclusively [31,32,50] or predominantly [9] in western countries. Differences in terms of culture and healthcare systems mean it is unwise to uncritically apply evidence for non-pharmacological interventions from resource rich countries to those that are resource poor. Our trial also differs from these studies in intervening at the level of the patient/carer dyad. Family carers are a crucial component in the delivery of care for people living with HIV/AIDS in Malawi and other similar African countries. Most pain management educational intervention studies have been conducted in cancer populations [36,51-53]. Our intervention is targeted at pain experienced by people living with HIV/AIDS. The intervention is simple and fits within a model of care where most healthcare contact is between patients and nurses and is supported by trained health assistants.

Trial status

The trial commenced recruiting in September 2012. We anticipate reaching our recruitment target by June 2013.

Abbreviations

AIDS: Acquired immunodeficiency syndrome; APCA: African palliative care association; ART: Antiretroviral therapy; BPI: Brief pain inventory; FPQ: Family pain questionnaire; PCRS: Picot caregiver rewards scale; POS: Palliative care outcomes scale; PPQ: Patient pain questionnaire; RCT: Randomised controlled trial; UNAIDS: United Nations Program of HIV and AIDS; WHO: World Health Organisation.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

KN, JS and AA were responsible for the development and refinement of the protocol. KN is the principal investigator and trial manager. KN will conduct data analysis under the supervision of AA. KN and AA wrote the initial draft of the manuscript. KN, JS and AA contributed to, edited and approved the final manuscript.

Acknowledgements

KN is funded by a doctoral scholarship from the School of Nursing, Midwifery and Physiotherapy, University of Nottingham; with additional financial support provided by the Malawi Government.
We thank all the patients and carers for their participation in the trial. We thank the clinic staff at both sites for assistance in recruitment. We thank Oscar Moyo and Amin Gondwe for conducting follow-up assessments.

Author details

[1]Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care, School of Nursing, Midwifery and Physiotherapy, University of Nottingham, Queen's Medical Centre, Nottingham NG7 2UH, UK. [2]School of Nursing Sciences, University of East Anglia, Norwich Research Park, Norwich NR4 7TJ, UK.

Received: 12 March 2013 Accepted: 3 July 2013
Published: 13 July 2013

References

1. World Health Organisation: *Global HIV/AIDS Response – Epidemic Update and Health Sector Progress Towards Universal Access – Progress Report.* Geneva: World Health Organization; 2011.
2. UNAIDS: *Global Report: UNAIDS Report on the Global AIDS Epidemic 2010.* Geneva: Joint United Nations Programme on HIV/AIDS (UNAIDS); 2010.
3. Callaghan M, Ford N, Schneider H: **A systematic review of task- shifting for HIV treatment and care in Africa.** *Hum Resour Health* 2010, **8:**8.
4. Lawson M, Mazengera S, Nkhoma-Mbawa F, Noel T: *Malawi Essential Health Services Campaign - Oxfam International Research Report.* Oxford, UK: Oxfam; 2008.
5. Makombe SD, Hochgesang M, Jahn A, Tweya H, Hedt B, Chuka S, Yu JK, Aberle-Grasse J, Pasulani O, Bailey C, Kamoto K, Schouten EJ, Harries AD: **Assessing the quality of data aggregated by antiretroviral treatment clinics in Malawi.** *Bull World Health Organ* 2008, **86:**310–314.
6. Ministry of Health and Population Malawi: *The Two Year Plan to Scale Up Antiretroviral Therapy in Malawi.* Llongwe, Malawi: Ministry of Health; 2004.
7. McCoy D: *HIV Care and Treatment in Southern Africa: Addressing Equity. EQUINET Discussion Paper Number 10.* EQUINET and OXFAM GB: Harare, Zimbabwe; 2003.
8. Sabin CA: **The changing clinical epidemiology of AIDS in the highly active antiretroviral therapy era.** *AIDS* 2002, **16**(Suppl 4):S61–S68.
9. Wantland DJ, Holzemer WL, Moezzi S, Willard SS, Arudo J, Kirksey KM, Portillo CJ, Corless IB, Rosa ME, Robinson LL, Nicholas PK, Hamilton MJ, Sefcik EF, Human S, Rivero MM, Maryland M, Huang E: **A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual.** *J Pain Symptom Manage* 2008, **36:**235–246.
10. Wahab KW, Salami AK: **Pain as a symptom in patients living with HIV/AIDS seen at the outpatient clinic of a Nigerian tertiary hospital.** *J Int Assoc Physicians AIDS Care (Chic)* 2011, **10:**35–39.
11. Oldham L, Kristjanson LJ: **Development of a pain management programme for family carers of advanced cancer patients.** *Int J Palliat Nurs* 2004, **10:**91–99.
12. Newshan G, Sherman DW: **Palliative care: pain and symptom management in persons with HIV/AIDS.** *Nurs Clin North Am* 1999, **34:**131–145.
13. Newshan G: **Pain in human immunodeficiency virus disease.** *Semin Oncol Nurs* 1997, **13:**36–41.
14. Harding R, Powell RA, Kiyange F, Downing J, Mwangi-Powell F: **Provision of pain- and symptom-relieving drugs for HIV/AIDS in sub-Saharan Africa.** *J Pain Symptom Manage* 2010, **40:**405–415.
15. Vogl D, Rosenfeld B, Breitbart W, Thaler H, Passik S, McDonald M, Portenoy RK: **Symptom prevalence, characteristics, and distress in AIDS outpatients.** *J Pain Symptom Manage* 1999, **18:**253–262.
16. Marcus KS, Kerns RD, Rosenfeld B, Breitbart W: **HIV/AIDS-related pain as a chronic pain condition: implications of a biopsychosocial model for comprehensive assessment and effective management.** *Pain Med* 2000, **1:**260–273.
17. Hughes J, Jelsma J, Maclean E, Darder M, Tinise X: **The health-related quality of life of people living with HIV/AIDS.** *Disabil Rehabil* 2004, **26:**371–376.

18. Hughes A: **Symptom management in HIV-infected patients.** *J Assoc Nurses AIDS Care* 2004, **15**(5 Suppl):7S–13S.
19. Hudson A, Kirksey K, Holzemer W: **The influence of symptoms on quality of life among HIV-infected women.** *West J Nurs Res* 2004, **26:**9–23. discussion 24–30.
20. Brechtl JR, Breitbart W, Galietta M, Krivo S, Rosenfeld B: **The use of highly active antiretroviral therapy (HAART) in patients with advanced HIV infection: impact on medical, palliative care, and quality of life outcomes.** *J Pain Symptom Manage* 2001, **21:**41–51.
21. Holzemer WL, Hudson A, Kirksey KM, Hamilton MJ, Bakken S: **The revised Sign and Symptom Check-List for HIV (SSC-HIVrev).** *J Assoc Nurses AIDS Care* 2001, **12:**60–70.
22. Grant L, Brown J, Leng M, Bettega N, Murray SA: **Palliative care making a difference in rural Uganda, Kenya and Malawi: three rapid evaluation field studies.** *BMC Palliat Care* 2011, **10:**8.
23. Namisango E, Harding R, Atuhaire L, Ddungu H, Katabira E, Muwanika FR, Powell RA: **Pain among ambulatory HIV/AIDS patients: multicenter study of prevalence, intensity, associated factors, and effect.** *J Pain* 2012, **13:**704–713.
24. Selwyn PA: **Why should we care about palliative care for AIDS in the era of antiretroviral therapy?** *Sex Transm Infect* 2005, **81:**2–3.
25. Solano JP, Gomes B, Higginson IJ: **A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease.** *J Pain Symptom Manage* 2006, **31:**58–69.
26. Peltzer K, Preez NF, Ramlagan S, Fomundam H: **Use of traditional complementary and alternative medicine for HIV patients in KwaZulu-Natal. South Africa.** *BMC Publ Health* 2008, **8:**255.
27. Heath KV, Montaner JS, Bondy G, Singer J, O'Shaughnessy MV, Hogg RS: **Emerging drug toxicities of highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection.** *Curr Drug Targets* 2003, **4:**13–22.
28. Harding R, Higginson IJ: **Palliative care in sub-Saharan Africa.** *Lancet* 2005, **365:**1971–1977.
29. Harding R, Karus D, Easterbrook P, Raveis VH, Higginson IJ, Marconi K: **Does palliative care improve outcomes for patients with HIV/AIDS? A systematic review of the evidence.** *Sex Transm Infect* 2005, **81:**5–14.
30. Long L, Fox M, Sanne I, Rosen S: **The high cost of second-line antiretroviral therapy for HIV/AIDS in South Africa.** *AIDS* 2010, **24:**915–919.
31. Goujard C, Bernard N, Sohier N, Peyramond D, Lancon F, Chwalow J, Arnould B, Delfraissy JF: **Impact of a patient education program on adherence to HIV medication: a randomized clinical trial.** *J Acquir Immune Defic Syndr* 2003, **34:**191–194.
32. Wu AW, Snyder CF, Huang IC, Skolasky R, McGruder HF, Celano SA, Selnes OA, Andrade AS: **A randomized trial of the impact of a programmable medication reminder device on quality of life in patients with AIDS.** *AIDS Patient Care STDS* 2006, **20:**773–781.
33. StataCorp: *Stata Statistical Software: Release 12.* College Station, TX: StataCorp LP; 2011.
34. Engel GL: **The need for a new medical model: a challenge for biomedicine.** *Science* 1977, **196:**129–136.
35. Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS: **Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain.** *Clin J Pain* 2004, **20:**309–318.
36. Clotfelter CE: **The effect of an educational intervention on decreasing pain intensity in elderly people with cancer.** *Oncol Nurs Forum* 1999, **26:**27–33.
37. Hudson PL, Aranda S, Hayman-White K: **A psycho-educational intervention for family caregivers of patients receiving palliative care: a randomized controlled trial.** *J Pain Symptom Manage* 2005, **30:**329–341.
38. Cleeland CS: *The Brief Pain Inventory User Guide.* Houston: The University of Texas M.D. Anderson Cancer Center; 2009.
39. Breitbart W: **Pain management and psychosocial issues in HIV and AIDS.** *Am J Hosp Palliat Care* 1996, **13:**20–29.
40. Beck SL, Falkson G: **Prevalence and management of cancer pain in South Africa.** *Pain* 2001, **94:**75–84.
41. Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, Kerns RD, Stucki G, Allen RR, Bellamy N, Carr DB, Chandler J, Cowan P, Dionne R, Galer BS, Hertz S, Jadad AR, Kramer LD, Manning DC, Martin S, McCormick CG, McDermott MP, McGrath P, Quessy S, Rappaport BA, Robbins W, Robinson JP, Rothman M, Royal MA, Simon L, *et al*: **Core outcome measures for chronic pain clinical trials: IMMPACT recommendations.** *Pain* 2005, **113:**9–19.
42. Ferrell BR, Ferrell BA, Ahn C, Tran K: **Pain management for elderly patients with cancer at home.** *Cancer* 1994, **74**(7 Suppl):2139–2146.
43. Harding R, Selman L, Agupio G, Dinat N, Downing J, Gwyther L, Mashao T, Mmoledi K, Moll T, Sebuyira LM, Panjatovic B, Higginson IJ: **Validation of a core outcome measure for palliative care in Africa: the APCA African Palliative Outcome Scale.** *Health Qual Life Outcomes* 2010, **8:**10.
44. Powell RA, Downing J, Harding R, Mwangi-Powell F, Connor S: **Apca: Development of the APCA African Palliative Outcome Scale.** *J Pain Symptom Manage* 2007, **33:**229–232.
45. Ferrell BA, Rhiner M, Rivera LM: **Development and evaluation of the Family Pain Questionnaire.** *J Psychosoc Oncol* 1993, **10:**21–35.
46. Picot SJ, Youngblut J, Zeller R: **Development and testing of a measure of perceived caregiver rewards in adults.** *J Nurs Meas* 1997, **5:**33–52.
47. Dworkin RH, Turk DC, Wyrwich KW, Beaton D, Cleeland CS, Farrar JT, Haythornthwaite JA, Jensen MP, Kerns RD, Ader DN, Brandenburg N, Burke LB, Cella D, Chandler J, Cowan P, Dimitrova R, Dionne R, Hertz S, Jadad AR, Katz NP, Kehlet H, Kramer LD, Manning DC, McCormick C, McDermott MP, McQuay HJ, Patel S, Porter L, Quessy S, Rappaport BA, *et al*: **Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations.** *J Pain* 2008, **9:**105–121.
48. Bennett MI, Bagnall AM, Jose Closs S: **How effective are patient-based educational interventions in the management of cancer pain? Systematic review and meta-analysis.** *Pain* 2009, **143:**192–199.
49. White IR, Horton NJ, Carpenter J, Pocock SJ: **Strategy for intention to treat analysis in randomised trials with missing outcome data.** *BMJ* 2011, **342:**d40.
50. Gifford AL, Laurent DD, Gonzales VM, Chesney MA, Lorig KR: **Pilot randomized trial of education to improve self-management skills of men with symptomatic HIV/AIDS.** *J Acquir Immune Defic Syndr Hum Retrovirol* 1998, **18:**136–144.
51. Lai YH, Guo SL, Keefe FJ, Tsai SL, Chien CC, Sung YC, Chen ML: **Effects of brief pain education on hospitalized cancer patients with moderate to severe pain.** *Support Care Cancer* 2004, **12:**645–652.
52. Du Pen SL, Du Pen AR, Polissar N, Hansberry J, Kraybill BM, Stillman M, Panke J, Everly R, Syrjala K: **Implementing guidelines for cancer pain management: results of a randomized controlled clinical trial.** *J Clin Oncol* 1999, **17:**361–370.
53. Lovell MR, Forder PM, Stockler MR, Butow P, Briganti EM, Chye R, Goldstein D, Boyle FM: **A randomized controlled trial of a standardized educational intervention for patients with cancer pain.** *J Pain Symptom Manage* 2010, **40:**49–59.

doi:10.1186/1745-6215-14-216
Cite this article as: Nkhoma *et al.*: An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: study protocol for a randomised controlled trial. *Trials* 2013 **14**:216.

Original Article

An Educational Intervention to Reduce Pain and Improve Pain Management for Malawian People Living With HIV/AIDS and Their Family Carers: A Randomized Controlled Trial

Kennedy Nkhoma, MSc, Jane Seymour, PhD, and Antony Arthur, PhD

Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care (K.N., J.S.), Division of Nursing, Queen's Medical Centre, Nottingham; and School of Health Sciences (A.A.), University of East Anglia, Norwich, United Kingdom

Abstract

Context. Advances being made in improving access to HIV drugs in resource-poor countries mean HIV patients are living longer, and, therefore, experiencing pain over a longer period of time. There is a need to provide effective interventions for alleviating and managing pain.

Objectives. To assess whether a pain educational intervention compared with usual care reduces pain severity and improves pain management in patients with HIV/AIDS and their family carers.

Methods. This was a randomized, parallel group, superiority trial conducted at HIV and palliative care clinics of two public hospitals in Malawi. A total of 182 adults with HIV/AIDS (Stage III or IV) and their family carers participated; carer participants were those individuals most involved in the patient's unpaid care. The educational intervention comprised a 30 minute face-to-face meeting, a leaflet, and a follow-up telephone call at two weeks. The content of the educational intervention covered definition, causes, and characteristics of pain in HIV/AIDS; beliefs and myths about pain and pain medication; assessment of pain; and pharmacological and nonpharmacological management. The primary outcome was average pain severity measured by the Brief Pain Inventory-Pain Severity subscale. Assessments were recorded at baseline before randomization and at eight weeks after randomization.

Results. Of the 182 patient/carer dyads randomly allocated, 157 patient/carer dyads completed the trial. Patients in the intervention group experienced a greater decrease in pain severity (mean difference = 21.09 points, 95% confidence interval = 16.56−25.63; $P < 0.001$).

Conclusion. A short pain education intervention is effective in reducing pain and improving pain management for Malawian people living with HIV/AIDS and their family carers. J Pain Symptom Manage 2015;■:■−■. © *2015 American Academy of Hospice and Palliative Medicine. Published by Elsevier Inc. All rights reserved.*

Key Words

HIV/AIDS, trial, pain, carers, educational intervention, palliative care

Introduction

Advanced HIV infection and its treatment with antiretroviral therapy are associated with physical and psychological symptoms.[1,2] These require focused assessment and management using locally available resources and interventions to optimize quality of life for patients and their carers.[1,3] The negative impact of pain on quality of life has been documented in many studies.[4,5] Pain is a major problem for people living with HIV/AIDS.[6–8] Pain is the most frequent and main cause of psychological distress.[9,10] Experiencing pain can reduce adherence to drug regimens and quality of life for HIV/AIDS patients.[11–15]

It is estimated that 35.3 million people were living with HIV/AIDS at the end of 2012.[16,17] In the same year, there were 1.6 million deaths from AIDS, a

Trial registration: Current Controlled Trials ISRCTN72861423.

Address correspondence to: Jane Seymour, PhD, Sue Ryder Care Centre for the Study of Supportive, Palliative and End of Life Care, Division of Nursing, Queen's Medical Centre, Nottingham, UK NG7 2UH. E-mail: jane.seymour@nottingham.ac.uk

Accepted for publication: January 7, 2015.

0885-3924/$ - see front matter
http://dx.doi.org/10.1016/j.jpainsymman.2015.01.011

reduction from 2.3 million deaths in 2005. In 2010, 1.4 million people began HIV medication, an increase in the number of people receiving treatment from the previous year of 27%. Greater access to effective treatment largely explains some of this decline in HIV/AIDS mortality.[18]

Sub-Saharan Africa has 10% of the world's population, but it is home to 69% of all people living with HIV/AIDS, making it the worst affected region.[16,17] Antiretroviral therapy can dramatically increase survival and years of healthy life, but is unavailable in many parts of the region.[18] In 2010 in sub-Saharan Africa, the number of individuals treated with antiretroviral medication increased from 37% in 2009[19] to 49% of the population eligible for treatment.[20]

In Malawi, the prevalence of HIV/AIDS is estimated at 11% of the population aged 15–49 years, with around 910,000 people living with HIV/AIDS at the end of 2011.[17] Approximately, 250 people are newly infected each day,[20] and at least 70% of Malawi's hospital beds are occupied by HIV/AIDS patients,[21] making Malawi the 12th worst affected country with HIV/AIDS worldwide.[22] However, there was a decline in HIV/AIDS prevalence from 14% in 2003 to 10% in 2011, predominantly because of increased access to antiretroviral therapy and preventive strategies.[23] Substantial progress has been made in the provision of HIV medication.[24] The involvement of nurses in the prescription and administration of medications and training health assistants to provide HIV counseling services have resulted in a greater proportion of patients starting HIV treatment within three weeks of diagnosis.[25] This has resulted in increased antiretroviral coverage to 67% in 2011.[23,24]

Adequate pain control remains a challenge for HIV/AIDS patients and has an impact on their quality of life.[13,14] Pain is experienced throughout the disease trajectory, severity being associated with later World Health Organization (WHO) clinical stage,[2,26–28] with an estimated 80% of people with advanced HIV infection experiencing severe pain.[29] Pain is also experienced as an effect of HIV medication.[30,31] With advances being made in improving access to HIV drugs in resource-poor countries, HIV patients are living longer and, therefore, experiencing pain over a longer period.[32,33] There is a need to provide effective interventions to HIV/AIDS patients in alleviating and managing pain. A systematic review[34] reported that self-management education programs for people living with HIV/AIDS results in short-term improvements in physical and psychosocial health and knowledge. However, all the trials reviewed were conducted in the U.S. and China where the health context is very different and none of these trials directly involved unpaid carers, a group likely to play a key role in the management of pain of those they care for.

Methods

Study Design

The pain education intervention study was a two-center, randomized, parallel group, wait-list controlled superiority trial. A detailed study protocol has been published.[35]

Setting and Participants

From October 2012 to June 2013, we recruited participants at HIV and palliative care clinics within two public hospitals (Ekwendeni and Mzuzu Central) in northern Malawi. Both hospitals provide inpatient, clinic-based and home-based care for people with HIV/AIDS that includes active treatment and palliative care. Participants were people living with HIV/AIDS who had a primary carer, who was identified as the individual most involved in their care. They were adults aged 18 years or older. All participants were able to read and write in English or Tumbuka (the vernacular language used in the northern part of Malawi). Participants were at WHO clinical stages III or IV of HIV/AIDS, or with a CD4 cell count of less than 350 cells, when the presence of pain and other symptoms is more likely because of opportunistic infections or side effects of HIV treatment. We excluded people living with HIV/AIDS if they had health problems that hindered cognition and communication such as HIV-associated dementia.

Recruitment

People living with HIV/AIDS in Malawi typically visit the hospital (palliative care and HIV clinics) with their family members. Posters about the study entitled "Pain Education Study" were prominently displayed in the clinics. Additionally, the first author (K. N.) or staff in these clinics informed patients about the study and provided them with information sheets. Potential participants were encouraged to discuss the study with family members before making a decision to take part. Those interested in taking part in the study were asked by K. N. to provide written informed consent. A checklist was used to confirm that all criteria for study eligibility were met.

Randomization, Concealment of Allocation, and Blinding

Baseline assessments were conducted by K. N. before randomization. Randomization was implemented by K. N. using opaque, sealed, and consecutively numbered envelopes. The envelope was opened in the presence of the participant. Participants had a 50% chance of

being allocated to either the pain education intervention group or usual care group. To limit imbalance between the treatment groups, participants were randomly assigned with block randomization using the "ralloc" command in Stata Version 12 (StataCorp LP, College Station, TX).[36] This allocates participants at random in blocks of sizes 2, 4, 6, 8, and 10, with block sizes allocated unequally in the ratio of 1:4:6:4:1 (Pascal's triangle).

Randomization was stratified by recruiting hospital. K. N. was not involved in the preparation of envelopes and was blinded to block size. A. A. prepared the envelopes and neither had contact with the study participants nor was he involved in recruitment. Owing to the nature of the intervention, participants and K. N. knew the treatment arm to which they were allocated, but the nurses who conducted follow-up outcomes were blinded to this information. Participants were told not to inform the assessors about treatment allocation. Assessors were asked if participants had told them of their group allocation after completion of outcome assessments to assess the success or failure of blinding.

Intervention and Comparator Groups

Pain Education Intervention. The nurse-led pain education intervention was informed by a biopsychosocial approach[37] to the management of pain among people with HIV/AIDS. It was designed to provide a systematic and proactive approach to assist people with HIV/AIDS and their carers to better understand and manage pain. The intervention consisted of a health education session delivered face-to-face by K. N., a Malawian registered nurse and specialist in palliative care, to the individual patient/carer dyads (Table 1). The face-to-face session took approximately 30 minutes in a quiet room within the palliative care or HIV/AIDS clinic where the participant was recruited. The components of the pain education intervention are listed in detail elsewhere[35] but included a discussion of HIV/AIDS-related pain, beliefs, and myths about pain and pain medication; ways to assess pain; and potential pharmacological and nonpharmacological methods to manage pain. A leaflet entitled "All About Your Pain" was given to participants, who were given the opportunity to look through it (Appendix, available at jpsmjournal.com). K. N. then discussed the contents of the leaflet with the participants and they were both encouraged to ask questions. Participants received a phone call reminder from K. N. after two weeks to inquire whether they had any further questions after the face-to-face discussion and reading the leaflet. Phone contacts typically lasted no more than five minutes. To minimize possible contamination between two groups, participants were asked not to share the leaflet with others. The features of usual care and the pain education intervention are explained in Table 1. There was no intention to systematically manage pain differently between the two groups, but one consequence for those in the pain education intervention group may have been to seek out additional treatments to manage their pain.

The leaflet drew on the evidence base and related literature for cancer pain management[5,38] and HIV/AIDS pain management in Africa[39,40] and pain management in Malawi.[41] Health care workers, HIV/AIDS patients, and family carers were involved in the development of the leaflet in terms of its design, content, technical characteristics, and readability.

The leaflet was in the form of a double-sided A4 page formatted so that it could be gate-folded into two for ease of use. It was printed in color and had illustrations to improve clarity and understanding. Diagrams and pictures were used to enhance understanding and to motivate the reader. The leaflet was pilot tested among 10 patients and 10 family carers to ensure that the content was readable and understandable.

Usual Care. Information relating to pain management is typically provided in a responsive rather than proactive manner and ad hoc rather than systematic,

Table 1
Features of Usual Care and the Pain Educational Intervention

Element	Usual Care/Wait-List Control	Pain Education Intervention
General description	Unstructured verbal information	Leaflet-based information, advice, explanation, and discussion
Form	General information on the treatment prescribed and instructions to be followed, responsive information from staff nurses	Information leaflet distributed "All About Your Pain" including 30 minute face-to-face verbal instructions and advice on pain assessment and management, phone call reminder after two weeks
Content	General information about HIV/AIDS medication and treatment compliance	Specific information about procedure on pain assessment and classification using pain scales and pain diagrams, including pain management using WHO analgesic ladder and specific drugs on each step
Written materials	None	Leaflet with simplified text information and diagrams, pictures/photos for quick reference
Method of delivery	General staff members	K. N.

WHO = World Health Organization.

with the focus restricted to pharmacological treatment of pain. Pain assessments are not usually conducted in a systematic way and not recorded routinely. It is unusual for this information to be routinely shared with patients and/or their carers.

Outcomes

The primary outcome was average pain severity measured using the Brief Pain Inventory (BPI; BPI-PS).[42] Secondary outcomes were pain interference with daily activities measured using the mean score of the seven pain interference items of the BPI (BPI-PI),[43] knowledge of pain management measured using the knowledge subscale of the Patient Pain Questionnaire (PPQ; PPQ-K),[44] and quality of life measured using the *African Palliative Care Association* (APCA) African Palliative Care Outcomes Scale (POS).[45,46] For carers, knowledge of pain management was measured using the knowledge subscale of the Family Pain Questionnaire (FPQ; FPQ-K),[47] carer motivation was measured using the Picot Caregiver Rewards Scale (PCRS),[48] and quality of life was measured using the APCA African POS.[45] All outcomes were self-reported. If participants were unable to self-complete after careful and standardized explanation of individual items, they were asked the question verbally and interviewers recorded their responses. Although the BPI[49] and APCA African POS[45] have both been used previously in sub-Saharan African populations, use of the PPQ, FPQ, and PCRS has been restricted to populations in Western countries. Our experience immediately before trial recruitment of piloting these scales as part of the questionnaire among 10 patients and 10 carers suggests that they are acceptable to and understood by members of the population of patients and carers from which our sample was recruited.

All outcome measures were conducted at baseline and eight weeks after delivery of the intervention. Eight weeks was considered sufficient time to observe any effect of the intervention and long enough to be considered clinically important. Outcomes were transposed to a zero to 100 scale, with higher scores indicating a more "positive" outcome; hence, a participant's individual score represented a percentage of the best possible score for that outcome.

Sample Size

We wished to be able to detect a mean difference of 10% between the treatment groups in the primary outcome measure (average pain severity on the BPI). A 10% improvement is considered the lower limit of change of clinical importance.[50] Using a *P*-value cutoff of 0.05 to determine a statistically significant result, 76 people per arm of the trial were needed to complete the study to give 80% power to detect such a difference. This is based on a review[51] that suggests that education-based interventions are able to produce this level of improvement in pain reduction, and that a standard deviation of 2.2 points is a liberal estimate of variability. To allow for 15% attrition, we aimed to recruit 182 participants to the trial.

Statistical Analysis

All patients and carers were analyzed according to the group to which they were randomized, although the use of strict intention-to-treat analysis is only possible where there is no loss to follow-up.[52,53] We compared treatment groups in terms of our primary outcome measure (average pain severity using the BPI-PS treated as a continuous measure) using a linear regression model, with baseline BPI-PS and treatment group and recruitment center as covariates. Analysis of each of the six secondary outcomes (BPI-PI, PPQ-K, APCA African POS patient score, FPQ-K, PCRS, and APCA African POS-carer score) were conducted using six equivalent models, with estimates of treatment effect conditional on the value of the outcome at baseline. Sensitivity analysis was performed as follows: we conducted secondary analyses that 1) adjusted for variables that were considered potential predictors of outcome (age, gender, and number of pain medications at baseline) assuming missing at random; and 2) considered plausible scenarios for departures from the missing at random assumption using the Stata command "rctmiss."[53] These scenarios were for all outcomes using scores of the mean outcome plus and minus 20 points for both arms and individual arms. All models included recruitment center as a covariate. All analyses were conducted using Stata Version 12.[36]

Ethical Approval

The study was approved by the University of Nottingham Medical School Research Ethics Committee (SNMP 11042012) and the National Health Sciences Research Committee of Malawi (NHSRC 1023).

Results

Of the 308 potential patient/carer dyads assessed, 182 were eligible, consented to participate, and completed the baseline measures (Fig. 1). A total of 92 were randomized to the pain education intervention and 90 were randomized to usual care. Of these, 15 patient/carer dyads and 10 carers were lost to follow-up. Reasons for attrition in the pain education group were patient having died before follow-up assessments ($n = 4$), no transport ($n = 2$), untraceable ($n = 1$), and moved away ($n = 1$). Reasons for attrition in the usual care group were: untraceable ($n = 2$),

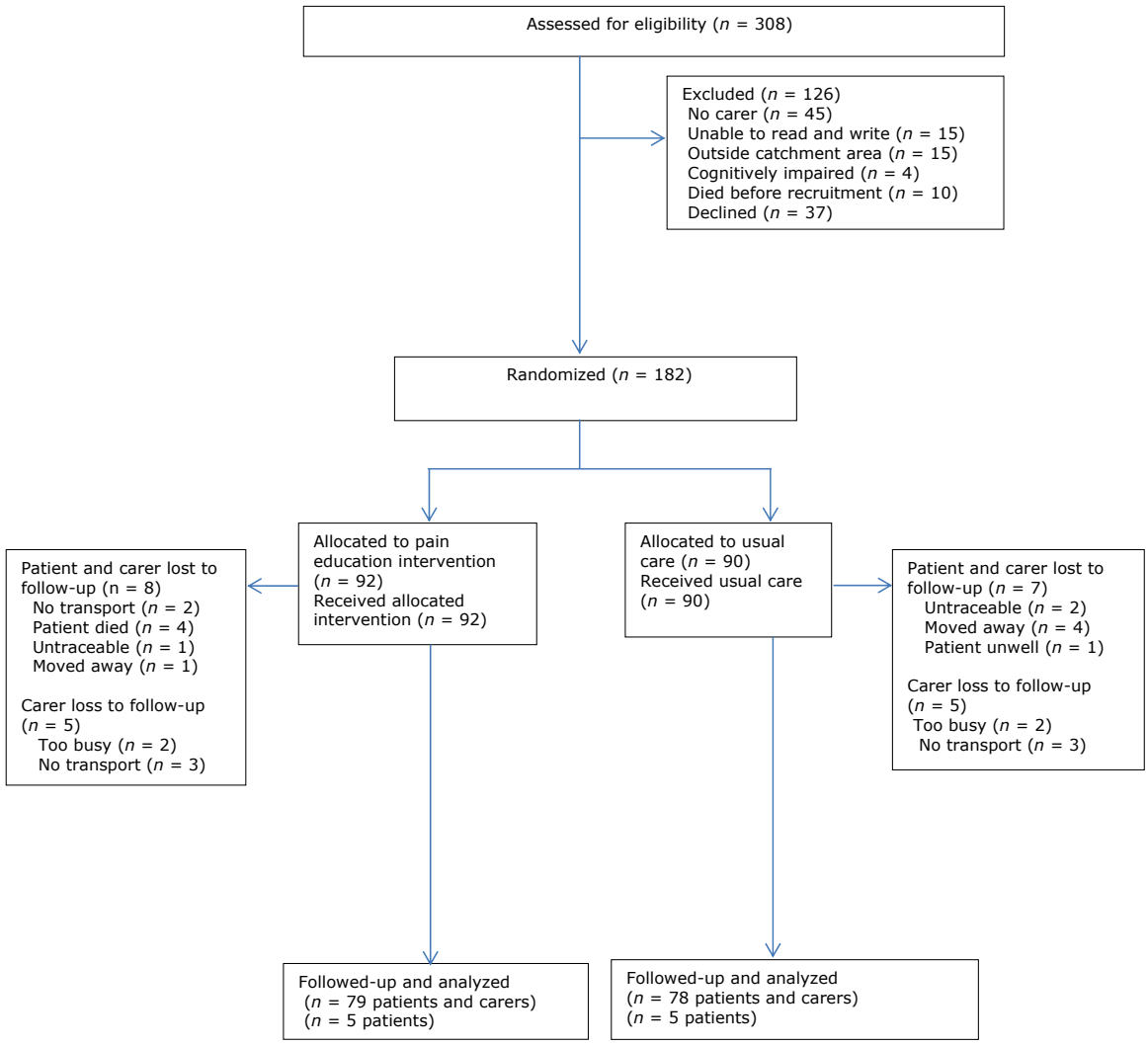


Fig. 1. Consolidated Standards of Reporting Trials (CONSORT) flow diagram of patients and carers throughout the study.

moved away ($n = 4$), and patient too unwell ($n = 1$). Reasons for carer loss to follow-up in the pain education group and usual care group were the same: carer too busy ($n = 2$) and no transport ($n = 3$). Of the 167 patients and 157 carers who completed the trial, complete data were available for all outcomes.

Baseline Characteristics

Pain education and usual care groups were similar at baseline in terms of sociodemographic profile except for gender; there were 43 (46.7%) male patients in the pain education group compared with 56 (62.2%) male patients in the usual care group (Table 2). There were also differences in carer relationship to the patient; there were 35 (38.0%) spousal carers in the pain education group and 44 (48.9%) spousal carers in the usual care group. At baseline, the two groups of patient/carer dyads were broadly similar in terms of the seven outcome measures.

Delivery and Receipt of the Intervention

The intervention was delivered by K. N. All the participants ($n = 92$) randomized to the pain education intervention attended a 30 minute face-to-face discussion and received a leaflet. Of these, 59 participants received the phone call reminder intervention at Week 2. Because of poor telephone network coverage, some participants did not receive a phone call ($n = 19$) but had physical contact with K. N. during their visit to the clinic at Week 2. Of the 59 participants who received a phone call, four also had face-to-face contact with K. N. at the clinic, where they were reminded to read the leaflet, and clarification was provided in response to their questions.

Primary Outcome

Both groups had reduced average pain severity at follow-up. However, those in the pain education group had a mean change of 40.95 (SD = 23.78), whereas the usual care group had a mean change of

Table 2
Baseline Characteristics of Participants ($N = 182$) Randomized to the Pain Education Intervention or Usual Care

Variables	Pain Education Intervention ($N = 92$), Mean (SD)	Usual Care ($N = 90$), Mean (SD)
Patient participants		
Age, yrs	40.5 (11.3)	41.3 (11.65)
Gender		
Male	43 (46.74)	56 (62.22)
Female	49 (53.26)	34 (37.78)
Marital status		
Married	61 (66.3)	58 (64.44)
Single	11 (11.96)	13 (14.44)
Divorced/separated	11 (11.96)	10 (11.11)
Widow/widower	9 (9.78)	9 (10)
Education		
Primary school	21 (22.83)	14 (15.56)
High school	66 (71.74)	72 (80)
College/university	5 (5.43)	4 (4.44)
BPI pain measures		
Average pain severity	50.76 (24.86)	51.22 (27.1)
Pain interference	49.91 (27.97)	49.46 (29.48)
Pain knowledge		
PPQ-K subscale	67.78 (16.61)	66.24 (18.84)
Quality of life		
APCA African POS subscale	44.78 (22.79)	48.92 (20.5)
Carer participants		
Age, yrs	41.1 (11.7)	42.6 (11.4)
Gender		
Male	14 (15.56)	19 (21.11)
Female	76 (84.44)	71 (78.89)
Marital status		
Married	78 (84.78)	81 (90)
Single	10 (10.87)	6 (6.67)
Divorced/separated	1 (1.09)	1 (1.11)
Widow/widower	3 (3.26)	2 (2.22)
Education		
Primary	21 (22.8)	22 (24.4)
High school	66 (71.7)	64 (71.1)
College/university	5 (5.4)	4 (4.4)
Carer relationship to patient		
Spouse	35 (38.04)	44 (48.9)
Sibling	27 (29.4)	20 (22.2)
Son/daughter	10 (10.9)	4 (4.4)
Friend	0	2 (2.2)
Parent	12 (13)	14 (15.6)
Other	8 (8.7)	6 (6.7)
Pain knowledge		
FPQ-K subscale	65.29 (16.93)	64.59 (18.53)
Motivation		
PCRS	78.91 (11.29)	79.41 (11.02)
Quality of life		
APCA African POS subscale	44.2 (18.95)	45.26 (18.55)

BPI = Brief Pain Inventory; PPQ-K = Patient Pain Questionnaire-Knowledge; APCA = African Palliative Care Association; POS = Palliative Care Outcomes Scale.

19.27(SD = 25.27; Table 3). When adjustments were made for baseline average pain severity score, recruitment center, age, gender, and number of pain medications, participants in the pain education group reported less severity of pain compared with those in the usual care group (mean difference = 21.25, 95% CI = 16.7−25.8; $P < 0.001$).

Secondary Outcomes

Participants in the pain education group had significantly less pain interference than the usual care group at follow-up (adjusted mean difference = 24.5, 95% CI = 19.61−29.38; $P < 0.001$). Patients in the pain education group reported greater improvement in knowledge than patients in the usual care group at follow-up (adjusted mean difference = 20.39, 95% CI = 17.51−23.27; $P < 0.001$). At follow-up, participants in the pain education group experienced better quality of life than participants in the usual care group (adjusted mean difference = 28.76, 95% CI = 24.62−32.91; $P < 0.001$; Table 3).

Carers in the pain education group reported greater improvement in knowledge than carers in the usual care group at follow-up (adjusted mean difference = 20.32, 95% CI = 17.37−23.28; $P < 0.001$; Table 4). Carers in the pain education group reported greater motivation to provide care than carers in the usual care group at follow-up (adjusted mean differenc = 7.64, 95% CI = 5.15−10.13; $P < 0.001$), as well as a better quality of life (adjusted mean difference = 34.16, 95% CI = 30.15−38.17; $P < 0.001$).

Sensitivity Analysis

In all the scenarios tested using various departures from the missing at random assumption, none altered the interpretation of better outcomes for the pain education group.

Discussion

In this randomized controlled trial, we found evidence that pain education intervention consisting of a face-to-face discussion, leaflet, and two-week follow-up phone call reduced pain severity, reduced pain interference with daily activities, improved patient knowledge of pain management, and patient quality of life. We also found evidence that the intervention improved carers' pain knowledge of pain management, quality of life, and motivation to provide care. The results are consistent with other studies of interventions to enhance self-care that have found improvement in pain management,[54,55] better knowledge about pain,[56–58] improved pain control,[55,56,59,60] and less pain interference with daily activities,[59,60] although the form, content, and context of these interventions were different and were administered among cancer patients. Our findings are different from those of a study conducted among HIV/AIDS patients[61] that found decreased quality of life when medication reminders were given, and to a trial that found no effect of an educational intervention to enhance self-management skills.[62]

Table 3
Patient Outcomes: Average Pain Severity on the BPI-PS for Pain Education and Usual Care Groups

Primary Outcome	Pain Education ($N = 84$)	Usual Care ($N = 83$)	Adjusted for Baseline Average Pain Severity and Recruitment Center		Adjusted for Baseline Average Pain Severity, Recruitment Center, Age, Gender, and Number of Pain Medications	
			Mean Difference (95% CI)	*P*-value	Mean Difference (95% CI)	*P*-value
BPI-PS subscale						
Mean (SD) average pain severity score						
At baseline ($n = 182$)	50.76 (24.86)	51.22 (27.1)				
At follow-up ($n = 167$)	92.62 (8.23)	71.69 (21.18)				
Mean change (SD) from baseline	40.95 (23.78)	19.27 (25.27)	21.09 (16.56–25.63)	<0.001	21.25 (16.7–25.8)	<0.001
Secondary Outcomes	**Pain Education ($N = 84$)**	**Usual Care ($N = 83$)**	**Adjusted for Baseline Score and Recruitment Center**		**Adjusted for Baseline Score, Recruitment Center, Age, Gender, and Number of Pain Medications**	
BPI-PI subscale						
Mean (SD) pain interference						
At baseline ($n = 182$)	49.91 (27.97)	49.46 (29.48)				
At follow-up ($n = 167$)	93.67 (9.33)	69.24 (25.21)				
Mean change (SD) from baseline	42.5 (25.91)	18.42 (23.92)	24.32 (19.33–29.32)	<0.001	24.5 (19.61–29.38)	<0.001
PPQ-K subscale						
Mean pain knowledge						
At baseline ($n = 182$)	67.78 (16.61)	66.24 (18.84)				
At follow-up ($n = 167$)	92.63 (8.16)	71.98 (15.21)				
Mean (SD) change from baseline	25.63 (15.5)	6.32 (11.00)	20.05 (17.25–22.86)	<0.001	20.39 (17.51–23.27)	<0.001
APCA African POS-patient subscale						
POS, mean (SD)						
At baseline ($n = 182$)	44.78 (22.79)	48.92 (20.5)				
At follow-up ($n = 167$)	90.58 (9.0)	63.37 (19.46)				
Mean (SD) change from baseline	45.44 (22.58)	14.46 (18.77)	28.32 (24.12–32.53)	<0.001	28.76 (24.62–32.91)	<0.001

BPI-PS/PI = Brief Pain Inventory-Pain Severity/Pain Interference; PPQ-K = Patient Pain Questionnaire-Knowledge; APCA = *African Palliative Care Association*; POS = Palliative Care Outcomes Scale.

Our finding of improved knowledge about pain among people with HIV/AIDS is consistent with a large trial[63] that found significant improvement in knowledge among HIV/AIDS participants after a HIV medication adherence intervention. The effect of the intervention on family carers is also consistent with other studies among family carers of people with cancer[64] and dementia.[65] Previous studies of family carers also found that family members feel rewarded and more prepared in their caregiving role if education is provided to them.[66,67]

Strengths and Limitations

To our knowledge, this is the first randomized controlled trial to be conducted in sub-Saharan Africa to recruit patient and carer dyads. The dearth of research into HIV/AIDS-related pain in African populations means that, for some outcomes, we have had to infer validity from validation studies conducted outside Africa. The sample size of 182 was larger than other trials of pain education interventions, which have, hitherto, been conducted in Western countries and targeting cancer patients[54,55,59] or cancer patients and their carers.[57,60] Recruitment to our trial was successful and attrition relatively low at 15% loss to follow-up. The main reasons for loss to follow-up were death of the patient, patient transferred to another center, lack of transport, and carer being too busy.

This was a complex intervention, and the nature of the intervention meant that it was not possible to blind participants of group allocation; we cannot exclude the possibility that patients and carers in the pain education intervention group may have responded more positively as a result of getting greater attention. However, social desirability bias is likely to have been limited by the use of staff nurses, blinded to allocation, conducting outcomes, although we cannot be sure that participants did not divulge that information.

The follow-up measures were conducted eight weeks after randomization; this was sufficient time to observe the effects of the intervention and is consistent with other pain education studies.[68,69] However, we do not know whether the positive results we observed are likely

Table 4
Carer Outcomes: Pain Knowledge, Motivation, and Quality of Life for Carer Participants

Outcomes	Pain Education ($N = 79$)	Usual Care ($N = 78$)	Adjusted for Baseline Score and Recruitment Center		Adjusted for Baseline Score, Recruitment Center, Age, Gender, and Number of Pain Medications	
			Mean Difference (95% CI)	*P*-value	Mean Difference (95% CI)	*P*-value
FPQ-K subscale						
Mean pain knowledge						
At baseline ($n = 182$)	65.29 (16.93)	64.59 (18.53)				
At follow-up ($n = 157$)	91.36 (7.8)	70.26 (15.88)				
Mean (SD) change from baseline	27 (15.8)	7.17 (9.8)	20.51 (17.58–23.44)	<0.001	20.32 (17.37–23.28)	<0.001
PCRS						
Mean (SD) motivation						
At baseline ($n = 182$)	78.91 (11.29)	79.41 (11.02)				
At follow-up ($n = 157$)	97.13 (5.87)	89.52 (11.14)				
Mean (SD) change from baseline	18.01 (11.96)	10.18 (8.48)	7.7 (5.26–10.14)	<0.001	7.64 (5.15–10.13)	<0.001
APCA African POS-carer subscale						
POS, Mean (SD)						
At baseline ($n = 182$)	44.2 (18.95)	45.26 (18.55)				
At follow-up ($n = 157$)	92.66 (8.84)	58.55 (17.94)				
Mean (SD) change from baseline	47.68 (18.86)	13.42 (16.63)	34.13 (30.16–38.09)	<0.001	34.16 (30.15–38.17)	<0.001

FPQ-K = Family Pain Questionnaire-Knowledge; PCRS = Picot Caregiver Rewards Scale; APCA = African Palliative Care Association; POS = Palliative care Outcomes Scale.

to be sustained beyond that time frame. Pain education participants were asked not to report the face-to-face discussion and not to pass the leaflet to any staff member or other patients to minimize contamination between two groups. However, the possibility of contamination cannot be excluded because participants lived in the same community where we had no means to prevent them from sharing the leaflet. Clustering the participants and randomizing according to some natural grouping such as area or clinic could have avoided contamination, thereby reducing Type II error,[70] but the scale of such a study would have required resources exceeding those available to us.

Conclusion

The current practice in HIV/AIDS and palliative care clinics in much of sub-Saharan Africa does not prioritize the provision of health-related information among patients. This study, conducted in Malawi, has provided strong evidence that a simple pain education intervention comprising a leaflet and verbal advice can reduce pain severity and interference, and improve pain knowledge and quality-of-life outcomes among HIV/AIDS patients. To build on these important findings, future research should include a health economic analysis. This would establish whether the benefits observed for patients and carers are accompanied by benefits to the wider health economy.

Disclosures Acknowledgments

Mr. Nkhoma is funded by a doctoral scholarship from the School of Health Sciences, University of Nottingham, with additional financial support provided by the Malawi Government. The authors declare no competing interests. The authors thank all the patients and carers for their participation in the trial and the clinic staff at both sites for assistance in recruitment. They thank Oscar Moyo and Amin Gondwe for conducting follow-up assessments.

References

1. Kell ME, Walley JD. Palliative care for HIV in the era of antiretroviral therapy availability: perspectives of nurses in Lesotho. BMC Palliat Care 2009;8:11.

2. Tapsfield JB, Bates MJ. Hospital based palliative care in sub-Saharan Africa; a six month review from Malawi. BMC Palliat Care 2011;10:12.

3. Wantland DJ, Holzemer WL, Moezzi S, et al. A randomized controlled trial testing the efficacy of an HIV/AIDS symptom management manual. J Pain Symptom Manage 2008;36:235–246.

4. Wahab KW, Salami AK. Pain as a symptom in patients living with HIV/AIDS seen at the outpatient clinic of a Nigerian tertiary hospital. J Int Assoc Physicians AIDS Care (Chic) 2011;10:35–39.

5. Oldham L, Kristjanson LJ. Development of a pain management programme for family carers of advanced cancer patients. Int J Palliat Nurs 2004;10:91–99.

6. Newshan G, Sherman DW. Palliative care: pain and symptom management in persons with HIV/AIDS. Nurs Clin North Am 1999;34:131–145.

7. Newshan G. Pain in human immunodeficiency virus disease. Semin Oncol Nurs 1997;13:36–41.

8. Harding R, Powell RA, Kiyange F, Downing J, Mwangi-Powell F. Provision of pain- and symptom-relieving drugs for HIV/AIDS in sub-Saharan Africa. J Pain Symptom Manage 2010;40:405–415.

9. Vogl D, Rosenfeld B, Breitbart W, et al. Symptom prevalence, characteristics, and distress in AIDS outpatients. J Pain Symptom Manage 1999;18:253–262.

10. Marcus KS, Kerns RD, Rosenfeld B, Breitbart W. HIV/AIDS-related pain as a chronic pain condition: implications of a biopsychosocial model for comprehensive assessment and effective management. Pain Med 2000;1:260–273.

11. Hughes J, Jelsma J, Maclean E, Darder M, Tinise X. The health-related quality of life of people living with HIV/AIDS. Disabil Rehabil 2004;26:371–376.

12. Hughes A. Symptom management in HIV-infected patients. J Assoc Nurses AIDS Care 2004;15(Suppl 5):7S–13S.

13. Hudson A, Kirksey K, Holzemer W. The influence of symptoms on quality of life among HIV-infected women. West J Nurs Res 2004;26:9–23; discussion 24–30.

14. Brechtl JR, Breitbart W, Galietta M, Krivo S, Rosenfeld B. The use of highly active antiretroviral therapy (HAART) in patients with advanced HIV infection: impact on medical, palliative care, and quality of life outcomes. J Pain Symptom Manage 2001;21:41–51.

15. Holzemer WL, Hudson A, Kirksey KM, Hamilton MJ, Bakken S. The revised Sign and Symptom Check-List for HIV (SSC-HIVrev). J Assoc Nurses AIDS Care 2001;12:60–70.

16. UNAIDS. UNAIDS report on the global AIDS epidemic 2013 2013;. Available at: http://www.unaids.org/en/resources/campaigns/globalreport2013/factsheet/. Accessed October 16, 2014.

17. World Health Organization. HIV Global update on HIV treatment: Results, impact and opportunities. Geneva, Switzerland: World Health Organization, 2013. Available at: http://apps.who.int/iris/bitstream/10665/85326/1/9789241505734_eng.pdf. Accessed October 22, 2014.

18. UNAIDS. UNAIDS report on the global AIDS epidemic 2010. Available at: http://www.unaids.org/globalreport/documents/20101123_GlobalReport_full_en.pdf. Accessed October 20, 2014.

19. Callaghan M, Ford N, Schneider H. A systematic review of task-shifting for HIV treatment and care in Africa. Hum Resour Health 2010;8:8.

20. WHO/UNAIDS/UNICEF. Global HIV/AIDS response: Epidemic update and health sector progress towards Universal Access 2011. Available at: http://www.who.int/hiv/pub/progress_report2011/en/. Accessed October 20, 2014.

21. Kumwenda JJ, Mateyu G, Kampondeni S, et al. Differential diagnosis of stroke in a setting of high HIV prevalence in Blantyre, Malawi. Malawi Med J 2005;17:107–111.

22. Lawson M, Messenger S, Nkhoma-Mbawa F, Noel T. Malawi essential health services campaign. Oxfam International Research Report. Oxford, UK: Oxfam International, 2008.

23. Malawi Government. Global AIDS response progress report: Malawi country: Report for 2010 and 2011 2012. Available at: http://www.unaids.org/sites/default/files/media_asset/20121120_UNAIDS_Global_Report_2012_with_annexes_en_1.pdf. Accessed October 18, 2014.

24. UNAIDS. Global Report: UNAIDS Report on the Global AIDS Epidemic 2012 2012. Available at: http://www.unaids.org/sites/default/files/en/dataanalysis/knowyourresponse/countryprogressreports/2012countries/ce_MW_Narrative_Report[1].pdf. Accessed September 16, 2014.

25. World Health Organisation. Global HIV/AIDS response—Epidemic update and health sector progress towards Universal Access—Progress report. Geneva, Switzerland: World Health Organization, 2011.

26. Grant L, Brown J, Leng M, Bettega N, Murray SA. Palliative care making a difference in rural Uganda, Kenya and Malawi: three rapid evaluation field studies. BMC Palliat Care 2011;10:8.

27. Namisango E, Harding R, Atuhaire L, et al. Pain among ambulatory HIV/AIDS patients: multicenter study of prevalence, intensity, associated factors, and effect. J Pain 2012;13:704–713.

28. Selwyn P. Why should we care about palliative care for AIDS in the era of antiretroviral therapy? Sex Transm Infect 2005;81:2–3.

29. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 2006;31:58–69.

30. Peltzer K, Preez NF, Ramlagan S, Fomundam H. Use of traditional complementary and alternative medicine for HIV patients in KwaZulu-Natal, South Africa. BMC Public Health 2008;8:255.

31. Heath KV, Montaner JS, Bondy G, Singer J, O'Shaughnessy MV, Hogg RS. Emerging drug toxicities of highly active antiretroviral therapy for human immunodeficiency virus (HIV) infection. Curr Drug Targets 2003;4:13–22.

32. Harding R, Higginson IJ. Palliative care in sub-Saharan Africa. Lancet 2005;365:1971–1977.

33. Harding R, Karus D, Easterbrook P, Raveis VH, Higginson IJ, Marconi K. Does palliative care improve outcomes for patients with HIV/AIDS? A systematic review of the evidence. Sex Transm Infect 2005;81:5–14.

34. Millard T, Elliott J, Girdler S. Self-management education programs for people living with HIV/AIDS: a systematic review. AIDS Patient Care STDS 2013;27:103–113.

35. Nkhoma K, Seymour J, Arthur A. An educational intervention to reduce pain and improve pain management for Malawian people living with HIV/AIDS and their family carers: study protocol for a randomised controlled trial. Trials 2013;14:216.

36. StataCorp LP. Stata statistical software: Release 12. College Station, TX: StataCorp LP, 2011.

37. Engel GL. The need for a new medical model: a challenge for biomedicine. Science 1977;196:129–136.

38. Scottish Intercollegiate Guidelines Network (SIGN). Cancer pain: Booklet for patients and carers. Edinburgh, UK: SIGN Executive, 2009:2–29.

39. African Palliative Care Association (APCA). A palliative care training manual: Community based caregivers in Africa. Kampala, Uganda: APCA, 2008:156–159.

40. African Palliative Care Association (APCA). Beating pain: A pocketguide for pain management in Africa. Kampala, Uganda: APCA, 2012:7–78.

41. Ministry of Health. Introduction to palliative care: Health professionals training manual. Lilongwe, Malawi: Ministry of Health, 2008:41–50.

42. Keller S, Bann CM, Dodd SL, Schein J, Mendoza TR, Cleeland CS. Validity of the brief pain inventory for use in documenting the outcomes of patients with noncancer pain. Clin J Pain 2004;20:309–318.

43. Dworkin RH, Turk DC, Farrar JT, et al. Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. Pain 2005;113:9–19.

44. Ferrell BR, Ferrell BA, Ahn C, Tran K. Pain management for elderly patients with cancer at home. Cancer 1994;74(Suppl 7):2139–2146.

45. Harding R, Selman L, Agupio G, et al. Validation of a core outcome measure for palliative care in Africa: the APCA African Palliative Outcome Scale. Health Qual Life Outcomes 2010;8:10.

46. Powell RA, Downing J, Harding R, Mwangi-Powell F, Connor S, APCA. Development of the APCA African Palliative Outcome Scale. J Pain Symptom Manage 2007;33:229–232.

47. Ferrell BR, Rhiner M, Rivera M. Development and evaluation of the Family Pain Questionnaire. J Psychosocial Oncol 1993;10:21–35.

48. Picot SJ, Youngblut J, Zeller R. Development and testing of a measure of perceived caregiver rewards in adults. J Nurs Meas 1997;5:33–52.

49. Beck SL, Falkson G. Prevalence and management of cancer pain in South Africa. Pain 2001;94:75–84.

50. Dworkin RH, Turk DC, Wyrwich KW, et al. Interpreting the clinical importance of treatment outcomes in chronic pain clinical trials: IMMPACT recommendations. J Pain 2008;9:105–121.

51. Bennett MI, Bagnall AM, Jose Closs S. How effective are patient-based educational interventions in the management of cancer pain? Systematic review and meta-analysis. Pain 2009;143:192–199.

52. Abraha I, Montedori A. Modified intention to treat reporting in randomised controlled trials: systematic review. BMJ 2010;340:c2697.

53. White IR, Horton NJ, Carpenter J, Pocock SJ. Strategy for intention to treat analysis in randomised trials with missing outcome data. BMJ 2011;342:d40.

54. Miaskowski C, Dodd M, West C, et al. Randomized clinical trial of the effectiveness of a self-care intervention to improve cancer pain management. J Clin Oncol 2004;22:1713–1720.

55. Yildirim YK, Cicek F, Uyar M. Effects of pain education program on pain intensity, pain treatment satisfaction, and barriers in Turkish cancer patients. Pain Manag Nurs 2009;10:220–228.

56. de Wit R, van Dam F, Zandbelt L, et al. A pain education program for chronic cancer pain patients: follow-up results from a randomized controlled trial. Pain 1997;73:55–69.

57. Wells N, Hepworth JT, Murphy BA, Wujcik D, Johnson R. Improving cancer pain management through patient and family education. J Pain Symptom Manage 2003;25:344–356.

58. Yates P, Edwards H, Nash R, et al. A randomized controlled trial of a nurse-administered educational intervention for improving cancer pain management in ambulatory settings. Patient Educ Couns 2004;53:227–237.

59. Oldenmenger WH, Sillevis Smitt PA, van Montfort CA, de Raaf PJ, van der Rijt CC. A combined pain consultation and pain education program decreases average and current pain and decreases interference in daily life by pain in oncology outpatients: a randomized controlled trial. Pain 2011;152:2632–2639.

60. Lin CC, Chou PL, Wu SL, Chang YC, Lai YL. Long-term effectiveness of a patient and family pain education program on overcoming barriers to management of cancer pain. Pain 2006;122:271–281.

61. Wu AW, Snyder CF, Huang IC, et al. A randomized trial of the impact of a programmable medication reminder device on quality of life in patients with AIDS. AIDS Patient Care STDS 2006;20:773–781.

62. Gifford AL, Laurent DD, Gonzales VM, Chesney MA, Lorig KR. Pilot randomized trial of education to improve self-management skills of men with symptomatic HIV/AIDS. J Acquir Immune Defic Syndr Hum Retrovirol 1998;18:136–144.

63. Goujard C, Bernard N, Sohier N, et al. Impact of a patient education program on adherence to HIV medication: a randomized clinical trial. J Acquir Immune Defic Syndr 2003;34:191–194.

64. Hudson P, Thomas T, Quinn K, Cockayne M, Braithwaite M. Teaching family carers about home based palliative care: final results from a group education program. J Pain Symptom Manage 2009;38:299–308.

65. Graff MJ, Vernooij-Dassen MJ, Thijssen M, Dekker J, Hoefnagels WH, Rikkert MG. Community based occupational therapy for patients with dementia and their care givers: randomised controlled trial. BMJ 2006;333:1196.

66. Henriksson A, Årestedt K, Benzein E, Ternestedt BM, Andershed B. Effects of a support group programme for patients with life-threatening illness during ongoing palliative care. Palliat Med 2013;27:257–264.

67. Northouse LL, Katapodi MC, Song L, Zhang L, Mood DW. Interventions with family caregivers of cancer patients: meta-analysis of randomized trials. CA Cancer J Clin 2010;60:317–339.

68. Clotfelter CE. The effect of an educational intervention on decreasing pain intensity in elderly people with cancer. Oncol Nurs Forum 1999;26:27–33.

69. Hudson P, Aranda S, Hayman-White K. A psycho-educational intervention for family caregivers of patients receiving palliative care: a randomised controlled trial. J Pain Symptom Manage 2005;30:329–341.

70. Torgerson DJ. Contamination in trials: is cluster randomisation the answer? BMJ 2001;322:355.