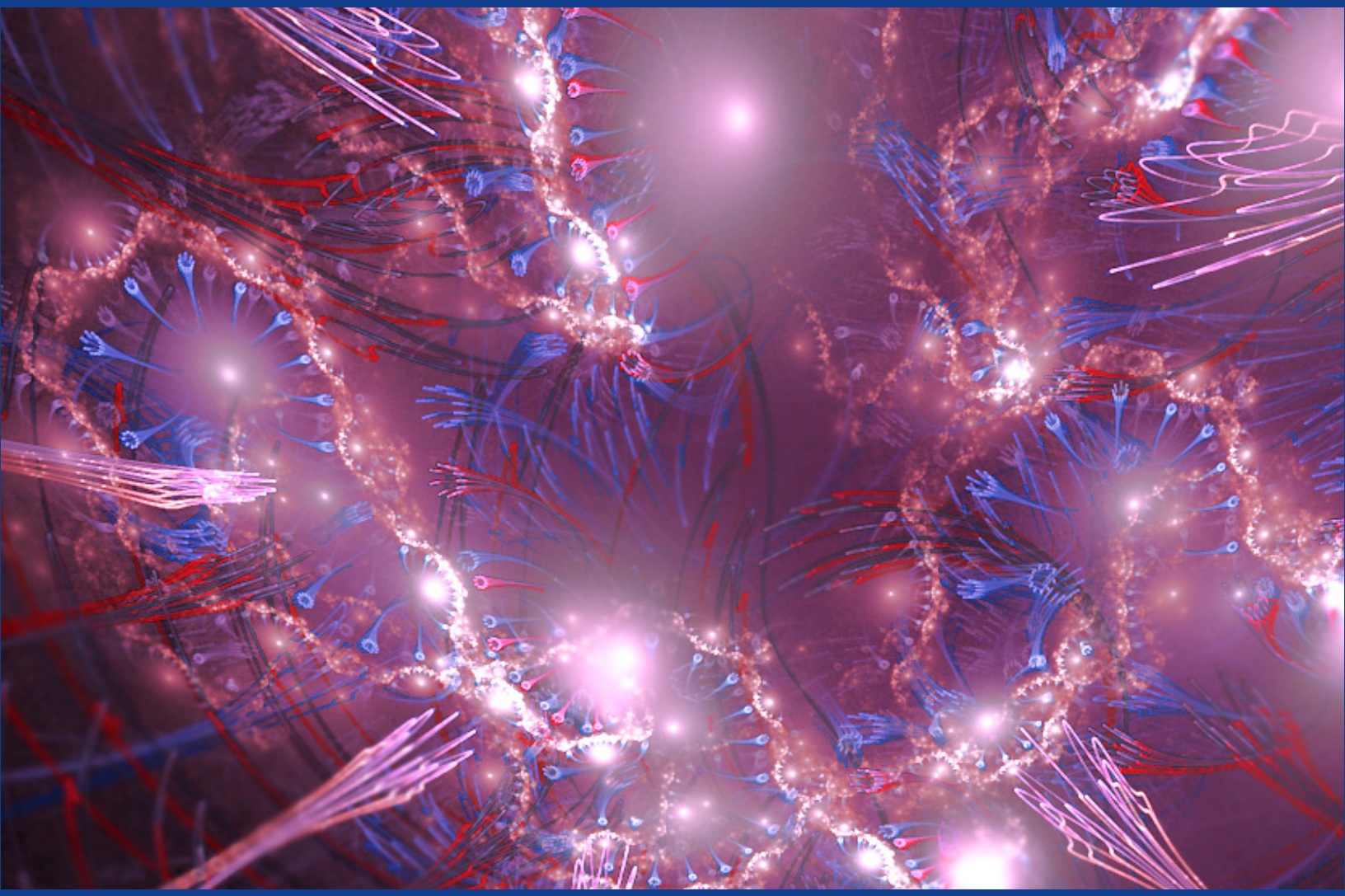
Pain Among HIV Outpatients Attending HIV Care and Support Facilities in Two East African Countries

SECONDARY ANALYSIS OF DATA FROM A PUBLIC HEALTH EVALUATION STUDY



MEASURE Evaluation
TECHNICAL REPORT

KING'S College LONDON

Pain Among HIV Outpatients Attending HIV Care and Support Facilities in Two East African Countries

SECONDARY ANALYSIS OF DATA FROM A PUBLIC HEALTH EVALUATION STUDY

Authors
Dr. Richard Harding
Dr. Vicky Simms
Dr. Lucy Selman

The Cicely Saunders Institute
Department of Palliative Care, Policy & Rehabilitation
King's College London
School of Medicine

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Executive Summary

Pain is a common and distressing symptom among people with HIV disease (1), yet despite cheap and effective availability of pain relief, it remains underreported and poorly controlled. The overall purpose of this study was to identify and characterize the prevalence and management of pain among HIV outpatients in PEPFAR sites in Kenya and Uganda. The study aimed to facilitate the development of enhanced pain management programmes in East Africa.

This report consists of extracted findings and secondary analysis of the PEPFAR Public Health Evaluation Study datasets. The analysis applied mixed methods to examine data at the facility level (n = 12), four one month apart surveys with HIV positive patients attending these facilities (n = 1337) as well as in-depth interviews (n = 189) with patients (n = 83), caregivers (n = 47) and facility staff (n = 50).

The study examined provision of five components of care related to pain management using the Client Services Receipt Inventory: assessment of pain, provision of strong and weak opioids and non-opioid analgesics, and treatment for neuropathic pain. Both data from service providers and outpatients were examined to present a complete picture of pain management by facility. In addition, country level longitudinal analysis of pain prevalence and management was conducted.

It was found that pain prevalence and management varied across facilities. Therefore, guidance on the assessment and treatment of pain is needed to reduce this inequity.

The analysis of pain management by country established that the overall trend in receipt of analgesics was decreasing over the course of the study. Non-opioid analgesics were received by over three-quarters of participants in each country and a similar proportion had their pain assessed. Receipt of other pain medication was rare. In both countries, a considerable proportion of pain management services were obtained from outside the study facility.

At the supply level, the data indicated the low availability of strong, and to a lesser degree, weak opioids. Opioids were more widely reported in Uganda than in Kenya. Stockouts were frequent.

The qualitative data revealed the interaction between physical, emotional, social and spiritual pain and described staff challenges in the assessment and management of the physical dimensions of pain. The analysis revealed that pain was an important issue to patients. A particularly important finding in the context of service delivery was that patients do not always report physical or psychosocial pain to healthcare staff. This suggests that eliciting patients' reports of pain in clinical practice may require in-depth probing and communication skills training.

Secondary analysis of patient data was conducted to examine changes in pain self reported over time. Pain was very highly prevalent over a four-month period, with over half (51%) of HIV outpatients experiencing severe pain during that time. During that four month period the proportion reporting severe pain reduced significantly, the proportion reporting moderate pain reduced slightly and the proportion reporting mild pain increased to more than half. Despite high pain prevalence, pain management was not a part of routine care. Thus, about 15% of people who had severe pain were never assessed during the four months of the study; only 9.5% received a weak opioid, 6.3% a strong opioid, and 22% treatment for neuropathic pain.

The study also analyzed various factors associated with the receipt of analgesia. Overall, receiving an opioid, non-opioid or neuropathic pain treatment was associated with higher odds of pain over time, even after adjusting for the pain score at baseline. Also, the study found that the receipt of analgesia was associated with demographic and clinical characteristics. Thus, patients with lower functional status and with a lower CD4 count had a higher chance of receiving opioids during the study. Older people and people with limited physical function had higher odds of receiving non-opioid analgesics.

In addition, the study examined patient characteristics that were associated with reporting severe pain. At the forth assessment, 16.5% of participants reported a severe combined pain score. It was found that people with impaired physical function and those in the lower wealth quintile had a higher probability of severe pain.

In the analysis of the relationship between pain and quality of life over time, it was established that pain was significantly associated with lower mental health score and physical health score after adjusting for baseline scores, functional status and wealth quintile.

This study revealed a high level of need for pain assessment and management at the facility and patient level. The integrated multiple data sources significantly underscored the need to enhance pain relief among East Africans attending PEPFAR sites for HIV care. Based on the findings of the study, the following recommendations were made: (i) to enhance the procurement, supply, necessary clinical training, prescribing, and stock control of analgesics; (ii) to make ongoing pain assessment as part of routine care and support, and to ensure adequate pain relief onsite, within health facilities; (iii) to initiate simple pain management audits to support improved pain management.

Section 1 Pain in HIV Disease

Pain is a common and distressing symptom among people with HIV disease (1), yet despite cheap and effective availability of pain relief, it remains underreported and poorly controlled.

Pain is prevalent throughout the disease trajectory, though particularly high in the later stages (2), and remains high for patients on antiretroviral therapy (ART) (3). However, despite the high prevalence and associated burden of pain among people with HIV disease, there has been a poor research and clinical focus on pain relief (4). Pain can be caused by the underlying disease, its consequences (e.g., opportunistic infections), treatment (e.g., antiretroviral therapy) or concurrent disorders.

1.1 PAIN AT DIAGNOSIS AND IN EARLY STAGES OF INFECTION

A high prevalence of burdensome physical and psychological symptoms is reported at all stages of HIV infection (5–8). A recent study reported 76% pain prevalence at the time of diagnosis in a sample of HIV/AIDS patients in rural Uganda (8). A recent systematic review of palliative care-related problems among people newly diagnosed with HIV (i.e., 0–6 months post-diagnosis) found a pain prevalence of 11–76% (9).

1.2 PAIN AND ART

Recent studies show that anti-retroviral treatment (ART) has not eliminated the need for effective pain and symptom control, given that problems (sometimes treatment-related) persist (10–12). Studies to establish potential correlates of the presence of pain in HIV have shown that the number of HIV-associated symptoms, disease stage, and use of ART are associated with pain prevalence (13–15).

Among UK outpatients on ART, data have revealed that pain and symptom burden is associated with increased sexual risk behaviour, viral rebound, poor adherence, and treatment switching (16–21). Within low-income settings with limited lines of treatment available, these carry serious implications for sustained control of viral replication.

A forthcoming systematic review has identified and appraised the evidence of palliative care-related problems among people on ART. A limitation of the current literature is that the source of pain is often unreported, whether originating from symptoms of opportunistic infections, HIV-related inflammation or side effects of specific ARVs (22, 23). Reported point prevalence of non-specified *pain* range from 19% (24) to 57.3% (11). The prevalence of muscle or joint pains ranged from 32.5% (25) to 72% (26).

African data suggest that pain prevalence does decrease, but persists following ART initiation, from 74% before ART to 32% three years after initiating treatment (27).

Depending on the definition of peripheral neuropathy used (i.e., pain due to nerve damage), prevalence is between 35% (28) to 60.8% (29) when one symptom of sensory neuropathy constitute the definition of a case. In terms of severity, a study in South Africa identified that 49% of all respondents had distal sensory neuropathy, i.e., reduced sensation of touch and ability to distinguish temperature. Among these, 70% were defined as moderately severe (30).

Peripheral neuropathy appears to persist despite effective viral control (31–33). In lower income countries risk factors for peripheral neuropathy among people on ART include TB, higher systolic blood pressure, older age, malnutrition and a CD4 count of less than 100 (30, 34).

1.3 PAIN IN ADVANCED DISEASE

Severe pain is experienced by 80% of those with advanced HIV/AIDS (35). One study of HIV-positive patients in South Africa who were receiving palliative care reported that 98% of patients experienced disease-related pain (36). Data from palliative care services in East and South Africa have reported that 82.6% of HIV patients reported pain (37). Patients with advanced disease are more likely to experience serious comorbidities such as organ failure and malignancies, which are also likely to cause pain (38).

1.3.1 Pain Assessment

The assessment of pain requires a detailed investigation of the sites, sensation and duration of the pain. Pain is a subjective experience, and the patient's report of their experience of pain should guide treatment. A holistic approach to pain is essential. Pain cannot be optimally controlled if other burdensome problems remain unaddressed, such as depression, hunger, etc. The African Palliative Care Association (APCA) *Guide to Beating Pain* in Africa (39) cites Dame Cicely Saunder's pioneering definition of pain—it is what the patient says hurts, and may have many sources both physical and non-physical. Their guidance gives further guidance on the assessment of pain as a first step in the sequential approach to assessment, measurement and management of pain.

The *Palliative Care Toolkit* (40) for limited resource settings also provides free resources for the assessment and management of pain, including sample documentation. Routine pain assessment within HIV clinical care is essential, as data suggest that HIV physicians tend not to detect their patients' problems (41, 42). This is compounded by HIV patients' belief that pain should be expected and endured (43).

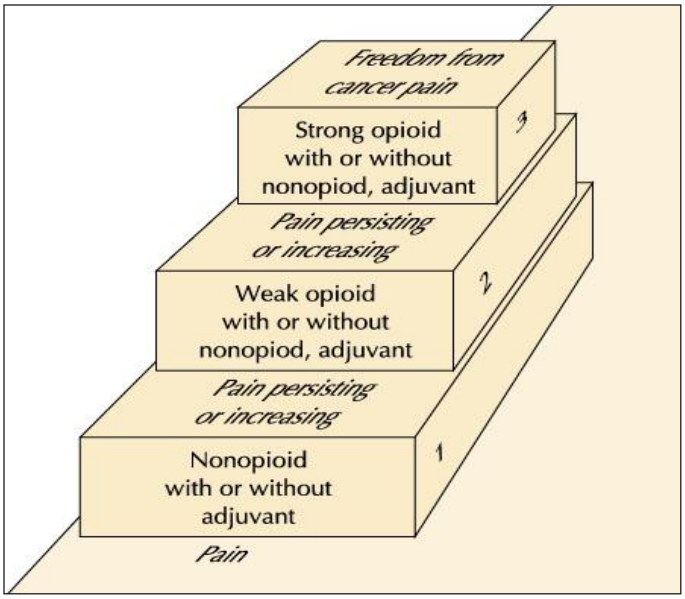
1.4 PAIN CONTROL

The WHO pain ladder (44) (Figure 1) outlines the need for non-opioid and opioid analgesics until pain has been controlled. Neuropathic pain, which is particularly common in people living with HIV (45) is caused by damage to nerves (from HIV disease and/or ART) and is only partially responsive to opioids. Barriers to opioid use include legal restrictions, unreliable supply, and a reluctance of health care staff to prescribe, based on fears of addiction and lethality. These myths can be overcome through education and training of both clinicians and policy makers, as advocacy can lead to policy change within Africa (46).

1.4.1 The Legal Context

Uganda was the first African country to have palliative care and pain relief in the National Health Plan. It has also successfully lobbied to the Government and initiated a change in the statute allowing Nurses and Clinical Officers who are trained in morphine use and palliative care to prescribe morphine (enacted 2004). They were the first African country to have achieved this. Morphine is free of charge for those who are prescribed by a registered prescriber. The register of prescribers is kept at the Palliative Care Association of Uganda (PCAU) and the Ministry of Health. Opioids are on the essential list of drugs for Kenya, and should be available up to the sub-district level hospital level, including for children. The law does not prohibit the licit use of opioids. However, only registered doctors can prescribe, and except for nurses trained in palliative care, nurses cannot prescribe.

Figure 1 The WHO Pain Ladder



Pain medications should be delivered by the mouth (i.e., orally); by the clock (i.e., regularly to prevent re-emergence of pain; and by the ladder (i.e., using the stepwise approach detailed in the figure).
Source: http://www.who.int/cancer/palliative/painladder/en

At the first level, drugs such as aspirin, paracetemol and non-steroidal anti-inflammatory drugs are required, and an adjuvant such as an anti-depressant may be necessary. At the second level, a weak opioid such as codeine is required, with the additional possibility of a non-opioid from the first level and/or an adjuvant. At the third level, opioids such as morphine are required, alongside potentially Step 1 and 2 analgesia and/or adjuvants.

A systematic review of the effectiveness of palliative care in the management of problems among persons with HIV found evidence that palliative care effectively controls pain (47). WHO indicated palliative care as an essential component of HIV management due to the burdensome problems experienced throughout the disease trajectory and alongside treatment (48). UNAIDS policy has also highlighted the need for palliative care in HIV patients way in advance of terminal care (49).

Figure 2 WHO Statement on HIV Palliative Care

> "Palliative care is an essential component of a comprehensive package of care for people living with HIV/AIDS because of the variety of symptoms they can experience—such as pain, diarrhoea, cough, shortness of breath, nausea, weakness, fatigue, fever, and confusion. Palliative care is an important means of relieving symptoms that result in undue suffering and frequent visits to the hospital or clinic. Lack of palliative care results in untreated symptoms that hamper an individual's ability to continue his or her activities of daily life. At the community level, lack of palliative care places an unnecessary burden on hospital or clinic resources." (50)

There has been significant progress in the availability of oral morphine for severe pain relief in Africa, with Uganda also having successfully lobbied for legislative change to enable nurses to prescribe opioids. Not only does this improve patient outcomes, these model projects have shown that opioids can be successfully purchased, stored and prescribed without diversion or addiction (51). However, even in services that focus on palliative care delivery in Africa, evidence shows patchy availability and unreliable supply of analgesia even at the first step of the WHO pain ladder (e.g., paracetemol) in African counties receiving funding from the United States President's Emergency Plan for AIDS Relief (PEFPAR) (52). All the required drugs for effective pain management are on the WHO essential (53) drugs list. Further guidance for the prescribing of opioids in Africa is given in the APCA guidance (54).

1.5 PATIENT-CENTERED EXPERIENCE OF PAIN

Disturbances in physical, psychological and social functioning have been found to be greater in patients experiencing pain compared to pain-free patients (55–60). Several studies have demonstrated the negative impact of pain on patient well-being (55, 59, 61, 62). The subjective nature of pain and the mediating role of ethnicity, culture and gender in pain affect perception (45, 63, 64).

Moreover, pain severity defined as the extent to which the patient's function is compromised is a primary factor determining the impact of pain on the patient (5). Intuitively, simple categorisations of *mild*, *moderate,* and *severe* are commonly used to guide clinical practice. Clinicians could potentially provide more effective treatment if there were a better understanding of what these ratings represent in terms of affect upon function, mental status and QOL. The World Health Organization (WHO) analgesic ladder follows a similar analogue for guidance on pain management (65).

The concept of *total pain* is useful when trying to define, assess, and manage pain in HIV-positive patients. HIV is clearly understood as impacting on the physical, psychological, social and spiritual domains of an infected person's life. *Total pain* was proposed as a way of understanding the subjective nature of pain—and that without attention to all domains of need it is unlikely that *pain* can be adequately reduced (66). This model of *total pain* has been successfully used to systematically review the needs of HIV patients, including physical pain, psychological distress, social and existential problems (9). This multidimensional approach to measuring patient outcomes is incorporated in the APCA African POS—a brief tool that measures all four dimensions of *total pain* in line with the WHO definition (67, 68).

1.6 SUMMARY

Pain cannot be controlled if it is not assessed during routine clinical care. A systematic review of the barriers and inequalities in HIV palliative care found an expectation among HIV patients that experience of uncontrolled pain is presumed to be a normal experience of the disease, that clinicians lack confidence in the assessment and treatment of pain, and that analgesia availability is sometimes limited (69). Even step 1 analgesics are often not available among services that specialise in HIV pain control in Africa, and the situation is worse for Step 2 and 3 analgesics. (4, 52, 70). All clinicians should be trained to assess pain among their patients irrespective of disease stage or treatment status. They also require the basic pain control skills that will enable their patients to live with chronic disease infection. For pain which appears complex to manage, HIV care facilities should have formal linkages with local pain specialist services (such as palliative care services) to assist in pain control. Lastly, all pharmacies should have analgesia available according to the WHO pain ladder.

Section 2 The PEPFAR Care and Support Public Health Evaluation

In 2003 the United States government (USG) funded a five-year, $15 billion initiative to combat the global HIV/AIDS epidemic: the President's Emergency Plan for AIDS Relief (PEPFAR). The funds were allocated approximately as follows: treatment (55%), prevention (20%), assisting orphans and vulnerable children (10%) and palliative care of individuals with HIV/AIDS (15%). For this funding, palliative care became defined as all HIV care. Palliative care was subsequently redefined as care and support by the US Office of Global AIDS Control (OGAC.)

PEPFAR commissioned a Public Health Evaluation (PHE) of care and support services in two African countries. The aims of the evaluation were

1. To describe the nature and scope of HIV care and support provision supported by PEPFAR in two African countries, including the types of facilities available, clients seen, and availability of specific components of care [Phase 1]. (71)
2. To evaluate how PEPFAR care and support programme components and costs are related to health outcomes [Phase 2]. (72)

Kenya and Uganda were chosen as the two countries. The design comprised two sequential periods of data collection using mixed methodologies. Phase 1 (2007) was a cross-sectional survey of facility configuration and activity using quantitative and qualitative descriptive data. Phase 2 (2008) was a longitudinal evaluation of existing care, focusing on outcomes of both new and existing adult patients in care and support services funded by PEPFAR using validated outcome tools (n = 1337 patients). Supplementary qualitative interviews with staff, patients and carers provided in-depth understanding of key issues (n = 173). An additional cost analysis component in this phase compared patient/family outcomes with their associated costs. Patient data collection for Phase 1 took place in 2007, Phase 2 was completed in 2008, and data collection for the costing component were collected in January 2009. The full protocol has been reported(73).

This report consists of extracted findings and secondary analysis of the PHE datasets to assemble findings related to the prevalence and management of pain.

Section 3 Methods

3.1 AIM AND OBJECTIVES

This analysis of the data aimed to determine the prevalence and experience of pain among HIV outpatients in PEPFAR sites in East Africa, and to facilitate the development of enhanced pain management programmes.
The specific objectives were to:

- fully utilise the large existing datasets in a way that offers maximum utility to the field audience,
- focus on key policy and programmatic questions,
- offer a more user friendly entry into the large PHE Phase 1 and 2 reports for each country (Kenya and Uganda),
- conduct secondary analysis of existing datasets to expand on the topic,
- wholly integrate the existing Phases and components of the PHE to provide triangulated insight into the clinical topic,
- develop a dissemination product to provide clear and concise summary of the findings and clinical directions for better care, and
- facilitate developments in specific clinical areas by care facilities through clear articulation of evidence.

3.2 INTEGRATION AND SECONDARY ANALYSIS OF PREVIOUS DATA

At the conclusion of the PHE, two separate reports were complied for the findings from Kenya and Uganda. For the present pain analysis, we have integrated and conducted secondary analysis from both PHE phases (i.e., Phase 1 in Kenya and Uganda, and Phase 2 in Kenya and Uganda). In the observational cohort, at least 100 participants at each of the 12 facilities were recruited to complete a battery of questionnaires four times at monthly intervals. These included the APCA African POS, a measure of multidimensional problems; the MOS-HIV, a quality of life questionnaire; the Client Services Receipt Inventory (CSRI) which had been completed by facility staff in Phase 1; and a demography questionnaire completed once only. The 35 questions of the MOS-HIV were converted into physical health and mental health summary scores using factor analysis (74).

The APCA African POS consists of seven questions addressed to the patient and three to the carer. The first question is ***please rate your pain in the last three days***. The item is scored from 0 = no pain to 5 = overwhelming pain. The tool has been validated in almost 700 patients across six African countries (67, 68).

Two MOS-HIV items directly relate to pain (75). They are:

- ***How much bodily pain have you generally had during the past thirty days?***
  None = 1; Very mild = 2; Mild = 3; Moderate = 4; Severe = 5; Very severe = 6
- ***During the past thirty days, how much did pain interfere with your normal work, including both work outside the home and housework?***
  Not at all = 1; A little bit = 2; Moderately = 3; Quite a bit = 4; Extremely = 5

The subset of Phase 1 data relating to the 12 Phase 2 facilities only was analysed for a description of care reported. The secondary analysis of the PHE findings addressed seven research questions, listed below.

1. ***Is the receipt of analgesia associated with demographic or clinical characteristics?***

   A variable was created, *receipt of opioid*, combining weak and strong opioids together. The three dichotomous outcomes (receipt of non-opioid, receipt of opioid and receipt of neuropathic treatment) were used in bivariate analysis to determine demographic variables associated with them. Each outcome was defined as receipt of the analgesic at any time during the study, therefore the data were analysed as cross-sectional using a period prevalence of four months. Variables found to be associated with the outcome in binary analysis were carried forward into a multivariate model using logistic regression, adjusting for facility using a fixed-effects logit model.

2. ***How does pain self-report change over time?***

   A variable was created to combine the three pain outcomes, using the coding in Table 1 below. The reason for this was to establish a combined pain score that was as sensitive as possible, to reduce the quantity of analysis and hence Type II error by combining all observations of pain into a single measure.

3. ***Is the receipt of analgesia associated with reduction in pain scores or improvement in quality of life over time?***

   To determine whether receipt of analgesia is associated with pain cross-sectionally a *maximum pain score* was generated, consisting of the highest combined pain score observed at any time point per person. Maximum pain score was tabulated against receipt of pain manag ement to identify the proportion of those with severe or moderate pain to receive treatment, as well as to ascertain an association between pain severity and use of management options.

Table 1 **Definition of *Maximum Pain* Variable**

Maximum Pain		POS 1		MOS-HIV 2		MOS-HIV 3
Severe	Has a score, at any time point, of	4, 5	or	5, 6	or	4, 5
Moderate	Worst score at any time point is	2, 3	or	3, 4	or	3
Mild	All scores at all timepoints are	0, 1	and	1, 2	and	1, 2

To determine whether pain is associated with analgesia over time, the combined score was converted into a binary variable, comparing those with no/mild pain (score 0) to those with moderate or severe pain (score 1). Mixed-effects multilevel logistic regression was used, with the binary combined pain score as an outcome. The covariates were receiving non-opioid analgesic,

receiving treatment for neuropathic pain, and receiving opioid. The two opioid items were combined into one due to the small numbers reporting either:

- ever having received analgesia during the period of study, as a covariate predicting change over time in pain score (three outcomes), PHSS, MHSS; or
- the time at which an opioids was received.

4. ***What are the themes connected to experiences of pain and pain management for HIV patients, family members and staff?***

   Thematic analysis of the qualitative data was used to answer this question. The full qualitative dataset of patients, families and staff was analysed to identify and themes relating to the experience or management of pain.

5. ***Is pain prevalence associated with demographic or clinical characteristics?***

   The combined pain score was used as the outcome for this question, converted into a binary variable (severe pain versus moderate/mild), compared to age, gender treatment and disease stage.

6. ***Is pain self-report associated with physical and mental quality of life over time?***

   Analysis of variance was used to compare mean physical and mental health summary scores by POS pain score and test for an association.

   To observe the relationship between pain report at baseline and quality of life over time, mean physical health score and mental health score were plotted by baseline (T0) combined pain score.

7. ***What predicts persistent pain after three months of care?***

   The combined pain score was used to identify people with severe pain after three months under care (T3.) Prevalence of severe pain at T3 was tabulated against demographic and clinical covariates, and time-series logistic regression was used to identify variables associated with the outcome, using the same method as for Question 1.

Facilities are coded by a letter A–M (missing out the letter I to avoid confusion with number 1). Facilities A–F are in Kenya, and G, H, J, K, L, and M are in Uganda. Data are initially analysed at the facility level as populations and practice differ by facility, and the analysis reveals these differences. Combined analysis would not allow us to discover variation at facility level, and would reduce the ability of the study to make recommendations to the field.

Section 4 Results 1: Integration of Previous Data

4.1 PHASE 1 PHARMACY STUDY

4.1.1 Reported availability of analgesia at different steps of WHO ladder

The Client Services Receipt Inventory (CSRI) included five components of care related to pain management: assessment of pain, provision of strong and weak opioids and non-opioid analgesics, and treatment for neuropathic pain. Table 2 shows availability of these components by facility, as reported by staff. The three options are for a care component to be available onsite (Y), not available at all (No) or avai lable only by referral (Ref). Only three facilities reported strong opioids and seven weak opioids, but all facilities had non-opioid analgesics and eleven had neuropathic pain treatment. Two facilities did not report that they conducted pain assessment. Opioids were more widely reported in Uganda than in Kenya.

Table 2 Availability of Pain Management

	Facility											
Component of Care	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**J**	**K**	**L**	**M**
Pain assessment	Y	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y
Strong opioids	N	N	N	N	N	N	Ref	Y	N	N	Y	Y
Weak opioids	N	N	N	Y	N	N	Y	Y	Y	Y	Y	Y
Non-opioids	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y	Y
Neuropathic pain treatment	Y	Y	Y	Y	Y	Y	Ref	Y	Y	Y	Y	Y

4.1.2 Comparison of Demand and Supply

Comparison of Table 2 and Table 3 shows that staff reports of care were not always commensurate with pharmacy stocks. Facilities H, L and M reported they provided strong opioids but only H and L had any morphine in stock. Codeine was more common than was reported. Ten facilities had codeine in the pharmacy, but only seven reported using weak opioids.

Table 3 Analgesic Pharmacy Stocks and Frequency of Stockouts

	A	B	C	D	E	F
Non-opioid tabs	75,000	0	1,000	15,014	6,500	3,800
Stockout	No	–	No	Yes	No	Yes
Non-opioid syrup	80,000	950k	4,500	13,500	9,200	2,540
Stockout	No	No	Yes	Yes	No	Yes
Codeine tabs	1,000	0	1,290	204	900	0
Stockout	No	–	No	Yes	No	–
Codeine syrup	0	0	0	0	0	0
Stockout	–	–	–	–	–	–
Morphine tabs	0	0	0	0	0	0
Stockout	–	–	–	–	–	–
Morphine syrup	0	0	0	0	0	0
Stockout	–	–	–	–	–	–
	G	**H**	**J**	**K**	**L**	**M**
Non-opioid tabs	237,000	5,500	750	107,000	5,223	3,000
Stockout	No	Yes	No	No	No	No
Non-opioid syrup	0	40,000	0	0	3,320	0
Stockout	–	No	–	–	Yes	
Codeine tabs	3,200	260	0	3,800	5,990	400
Stockout	No	Yes	–	No	No	Yes
Codeine syrup	0	0	1,000	0	0	0
Stockout	–	–	Yes	–	–	–
Morphine tabs	0	170	0	0	0	0
Stockout	–	No	–	–	–	–
Morphine syrup	0	0	0	0	1,190	0
Stockout	–	–	–	–	Yes	–

4.1.3 Detail on Stockouts

The survey team asked whether each drug had been out of stock in the six months prior to the survey. Table 3 shows that stockouts were frequent. For non-opioid tabs the prevalence of stockout was 27% (three out of eleven), for non-opioid syrup 50% and for codeine tabs 33%. Codeine syrup and morphine syrup were only available at one site each, and in both cases had been out of stock recently.

4.1.4 Is Step 3 Analgesia Availability Related to Availability of Other Medical Specialties?

Two facilities carried Step 3 analgesia: facility H had 170 morphine tablets in stock and facility L had 1190 mls of morphine syrup.

4.2 PHASE 2 QUANTITATIVE COHORT

4.2.1 Description of Sample

The Phase 2 quantitative cohort recruited 1337 HIV positive outpatients. Their demographic profile is described in Table 4. At all facilities the majority of participants were female, ranging from 57.7% to 78.5%. The modal age group was 30–39 for all facilities except two, where more participants were aged 18–29. In most facilities the majority had primary education. Four facilities (A, F, G and H) had a poorer than average population and three (D, J and K) had a population that was better off than average. In Facility G, 80.4% of the sample was in the lowest quintile.

The proportion of newly diagnosed participants varied widely from none to 70.8%. The proportion on ART was also highly variable, from 8.3% to 91.6%. At eight facilities over 85% of participants had a CD4 test result but the other four varied from 33.6% to 50.4%. At nine facilities the majority of people had the best possible score for functional status (0) as measured by the ECOG functional status scale, which is a commonly used tool that has been shown to operate separately from measures of quality of life and psychosocial function(76, 77). At Facility G 42.0% scored 2, 3, or 4 for functional status, whereas at all other facilities the maximum was 13.1%.

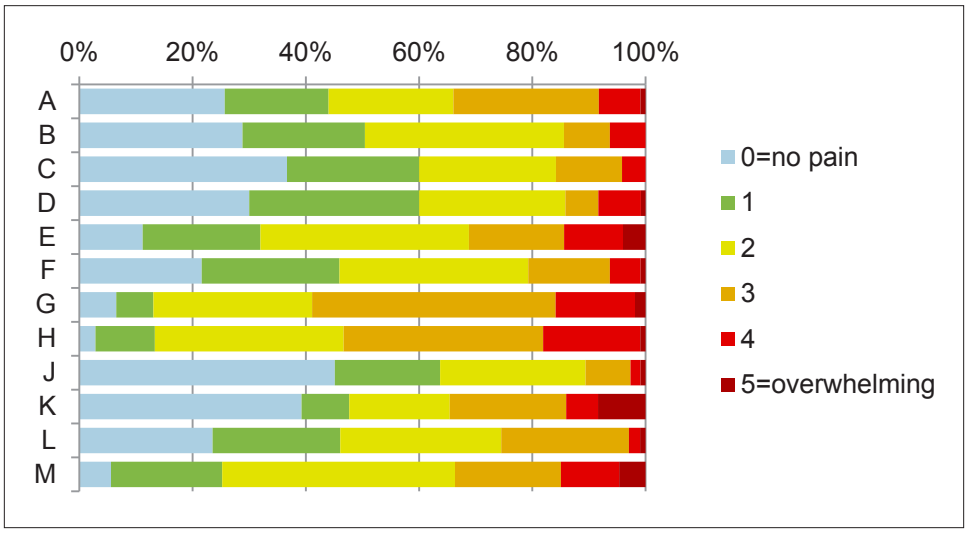
Table 4: Demography by Country (%)

Demographic		A (n = 109)	B (n = 111)	C (n = 120)	D (n = 120)	E (n = 125)	F (n = 111)	G (n = 107)	H (n = 105)	J (n = 112)	K (n = 107)	L (n = 102)	M (n = 107)
Gender	Female	68.8	74.8	65.8	72.5	70.4	57.7	78.5	64.8	60.7	61.7	71.6	72.0
Age	18–29	44.0	12.6	35.0	34.2	27.2	30.9	16.8	14.3	43.8	32.7	29.4	38.3
	30–39	32.1	43.2	41.7	47.5	45.6	42.7	40.2	39.1	37.5	47.7	44.1	38.3
	40–49	12.8	30.6	15.8	13.3	21.6	22.7	32.7	38.1	15.2	15.9	24.5	15.9
	50–59	8.3	9.9	7.5	5.0	5.6	2.7	6.5	6.7	3.6	1.9	2.0	6.5
	60–70	2.8	3.6	0.0	0.0	0.0	0.9	3.7	1.9	0.0	1.9	0.0	0.9
Education	None	5.6	2.7	1.7	5.0	2.4	0.9	25.2	14.3	4.5	3.7	6.9	8.4
	Began primary	69.4	54.1	55.8	50.0	40.8	54.1	53.3	57.1	35.7	57.9	37.3	53.3
	Began secondary	22.2	38.7	30.8	37.5	46.4	37.8	20.6	25.7	48.2	26.2	39.2	27.1
	Diploma+	2.8	4.5	11.7	7.5	10.4	7.2	0.9	2.9	11.6	12.2	16.7	11.2
Wealth quintile	Lowest	39.5	2.7	5.0	1.7	15.2	37.3	80.4	43.8	2.7	3.7	5.9	19.6
	Second	32.1	27.0	25.8	3.3	14.4	24.6	6.5	47.6	4.5	10.3	8.8	26.2
	Middle	19.3	33.3	15.8	15.0	33.6	19.1	10.3	4.8	19.6	23.4	15.7	27.1
	Fourth	8.3	19.8	21.7	28.3	21.6	12.7	1.9	2.9	42.9	30.8	30.4	17.8
	Highest	0.9	17.1	31.7	51.7	15.2	6.4	0.9	1.0	30.4	31.8	39.2	9.4
Newly diagnosed	Yes	36.7	2.7	63.3	54.2	19.2	35.1	0.0	17.1	70.8	25.2	34.3	29.0
On ART during study	Yes	66.7	67.6	8.3	40.0	56.5	31.5	91.6	36.2	8.9	14.0	38.2	60.8
Functional status	0	56.0	74.8	80.0	75.0	58.4	71.2	20.6	79.1	82.3	51.4	43.1	23.4
	1	33.9	22.5	19.2	20.8	34.4	20.7	37.4	19.1	9.7	43.9	45.1	63.6
	2	9.2	2.7	0.8	4.2	6.4	7.2	38.3	0	4.4	2.8	8.8	8.4
	3 or 4	0.9	0.0	0.0	0.0	0.8	0.9	3.7	1.9	3.5	1.9	2.9	4.7
Had CD4 test	Yes	88.1	91.0	85.8	99.2	90.4	89.2	100.0	41.0	50.4	46.7	90.2	33.6
CD4 count	0–100	16.7	2.0	29.1	27.6	13.3	15.2	9.4	9.3	12.3	16.0	20.7	8.3
	101–200	15.6	19.8	19.4	19.8	17.7	24.2	30.8	7.0	10.5	20.0	16.3	13.9
	201–350	28.1	37.6	20.4	21.6	29.2	21.2	36.5	30.2	22.8	36.0	22.8	36.1
	350+	39.6	40.6	31.1	31.0	39.8	39.4	23.4	53.5	54.4	28.0	40.2	41.7

4.2.2 Prevalence of Pain Using Two Measures (APCA African POS & MOS-HIV)

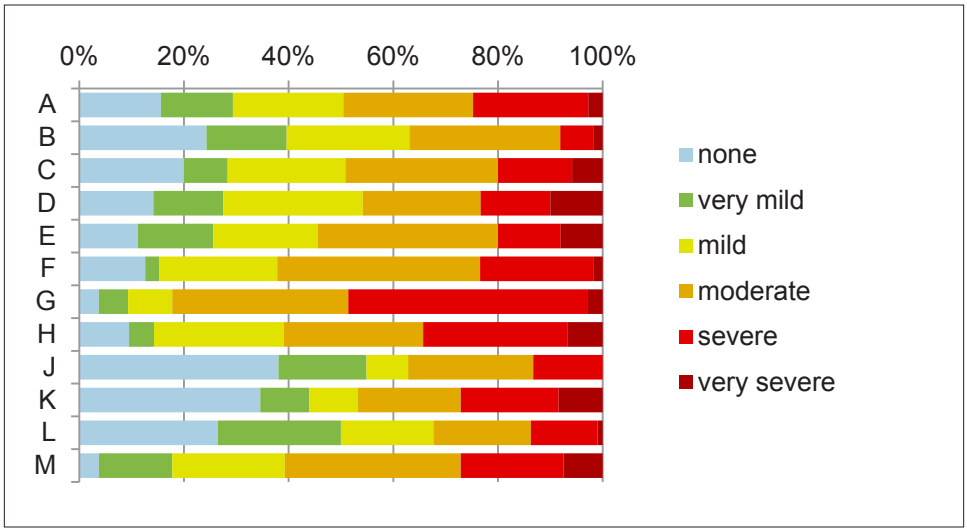
Figure 3, Figure 4 and Figure 5 below display the distribution of the three pain outcome scores for these participants at recruitment.

Figure 3 POS Pain Scores at T0: *Please rate your pain in the last three days*



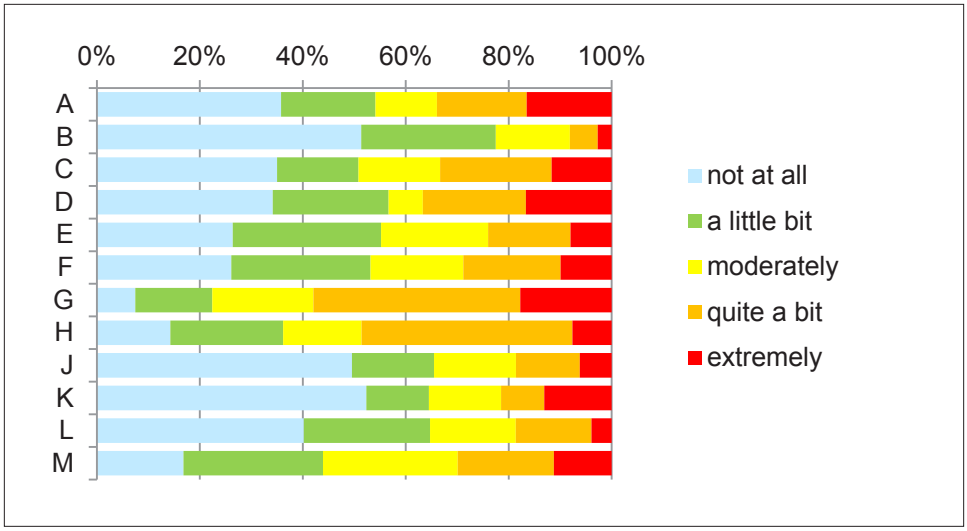
At all facilities, the majority of participants reported pain. Severe pain was most prevalent in Facilities G and H, where the median score was 3. The highest prevalence of overwhelming pain was in Facilities K, E and M.

Figure 4 MOS-HIV Question 2 at T0: *How much bodily pain have you generally had during the past thirty days?*



Scores are higher in Figure 2 than Figure 1, indicating more prevalent and severe pain. The MOS-HIV question includes pain within thirty days rather than three. These findings suggest that for some people, pain is acute rather than chronic, as prevalence is greater over a longer period of time. Pain is most severe among patients in Facility G, followed by F, H, and M.

Figure 5 **MOS-HIV Question 3 at T0: *During the past thirty days, how much did pain interfere with your normal work?***



Scores for the extent to which pain interfered with daily living were lower than those for pain experience, but at nine facilities the majority of participants found that pain did interfere with their lives to some extent. Almost 20% said pain interfered extremely at Facilities A, D, and G.

4.2.3 Pain Management by Country

Table 5 **Percentage of Participants Receiving Each Component of Care During the Study (in Descending Order of Most Commonly Ever Received)**

	Kenya (n = 641)					Uganda (n = 696)				
Component of Care	**T0**	**T1**	**T2**	**T3**	**Ever**	**T0**	**T1**	**T2**	**T3**	**Ever**
Non-opioid analgesics	46.9	43.6	41.4	41.3	78.3	56.7	54.5	49.4	43.7	82.8
Assessment of pain	42.4	46.9	43.4	43.2	75.9	38.0	50.9	44.8	40.5	76.0
Treatment for neuropathic pain	6.2	5.7	4.1	4.4	14.2	6.1	8.6	6.4	6.3	17.8
Weak opioids	3.2	1.6	1.5	0.0	5.3	4.4	2.8	1.5	1.3	8.4
Strong opioids	2.5	1.7	0.8	0.0	4.5	2.8	1.3	1.5	0.6	5.3
Any component	59.2	59.5	55.3	54.2	87.2	62.7	65.5	59.2	51.9	87.1

Table 5 shows that all care components become less frequent over time, with the exception of pain assessment, which is more likely at T1 than T0. Treatment with non-opioid analgesics is always slightly more common than pain assessment. Non-opioid analgesics were received by over three-quarters of participants in each country and a similar proportion had their pain assessed. Receipt of other pain medication was rare. The overall trend in receipt of analgesics was decreasing over the course of the study.

In both countries the prevalence of pain care decreased moderately over time. The probability of receiving pain care during the study period was almost exactly the same in the two countries (87.1% and 87.2%).

Table 6 Percentage of People Receiving Care at the Facility and Elsewhere, Kenya

	T0 (n = 696)		T1 (n = 634)		T2 (n = 613)		T3 (n = 592)	
Component of Care	fac	else	fac	else	fac	else	fac	else
Assessment of pain	31.2	11.1	42.7	4.1	40.5	2.8	40.0	3.2
Non-opioids	24.9	21.6	31.9	11.5	29.7	11.6	28.9	12.3
Treatment for neuropathic pain	3.9	2.3	4.7	0.9	3.8	0.3	3.5	0.8
Weak opioids	1.6	1.6	1.1	0.5	1.1	0.3	0.0	0.0
Strong opioids	1.4	1.0	1.1	0.6	0.7	0.2	0.0	0.0

Table 6 shows that in Kenya a considerable proportion of pain management services were obtained from outside the study facility. Pain assessment was normally done by the facility but after the first month around 11–12% of non-opioid analgesics were procured elsewhere (i.e. not from the facility under study). Table 7 shows that in Uganda this effect was even more common. Weak opioids were almost as likely to come from outside the facility as to be provided by it.

Table 7 Percentage of People Receiving Care at the Facility and Elsewhere, Uganda

	T0 (n = 641)		T1 (n = 615)		T2 (n = 583)		T3 (n = 538)	
Component of Care	fac	else	fac	else	fac	else	fac	else
Assessment of pain	26.3	11.7	42.1	8.8	35.3	9.4	31.0	9.5
Non-opioids	27.0	29.7	38.4	16.1	35.7	13.7	31.6	12.1
Treatment for neuropathic pain	4.1	2.0	7.5	1.1	5.0	1.4	5.8	0.6
Weak opioids	2.2	2.2	1.6	1.1	0.9	0.7	0.9	0.4
Strong opioids	0.8	2.0	0.5	0.8	0.3	1.2	0.4	0.2

4.2.4 Pain Management by Facility

Table 8 shows the patients who received morphine from the PEPFAR-funded facilities. In Phase 1, facilities H, L, and M said they offered strong opioids, and only facilities H and L had morphine in stock. As Table 9 shows, over half of patients who received morphine (55%) were at Facility E, which had not reported morphine, and facilities B, G, and J also provided morphine to at least one patient each.

Table 8 Record of Patients Receiving Morphine from the Facility

Patient	Facility	T0	T1	T2	T3
1	B	Yes	No	No	No
2	D	Yes	Yes	No	No
3	D	Yes	No	No	No
4	E	No	Yes	No	No
5	E	Yes	No	No	No
6	E	Yes	No	No	No
7	E	Yes	No	No	No
8	E	Yes	No	No	No
9	E	No	Yes	No	No
10	E	No	No	Yes	No
11	E	No	No	Yes	No
12	E	No	Yes	No	No
13	E	No	Yes	No	No
14	E	Yes	-	-	-
15	E	No	Yes	No	No
16	E	Yes	No	No	No
17	E	No	No	Yes	No
18	E	No	No	Yes	
19	E	Yes	No	No	No
20	E	No	Yes	No	No
21	G	Yes	No	-	-
22	G	Yes	Yes	No	No
23	G	No	Yes	No	No
24	G	No	Yes	No	No
25	G	Yes	No	No	No
26	H	Yes	No	No	No
27	H	No	No	Yes	No
28	H	Yes	No	No	No
29	J	No	No	Yes	-
30	L	No	No	No	Yes
31	L	No	No	No	Yes
		15	**10**	**6**	**2**

Table 9 shows that the prevalence of care components varied by facility, but the relative frequency usually did not. The prevalence of pain assessment at any time ranged from 45.1% to 96.3%. At five facilities no patients received a strong opioid and the highest prevalence by some distance was 21.6% at Facility E. At two of the five without strong opioids, no patients received weak opioids either, and again prevalence was highest at Facility E (17.6%). Over 60% of patients received a non-opioid analgesic at all facilities. At all facilities the majority of participants received at least one element of pain assessment or management during the study, with Facility J the lowest at 66.4%.

Table 9 Percent of Participants Ever Receiving Components of Care by Facility

Component of Care	A	B	C	D	E	F	G	H	J	K	L	M
Assessment of pain	94.5	46.8	70.0	84.2	68.8	91.9	96.3	85.7	45.1	84.1	56.9	88.8
Strong opioids	0.0	0.9	0.0	2.5	21.6	0.0	4.7	11.4	13.3	0.0	2.0	0.0
Weak opioids	3.7	3.6	1.7	4.2	17.6	0.0	12.1	9.5	13.3	0.0	13.7	1.9
Non-opioids	82.6	65.8	65.8	86.7	80.8	88.3	100.0	94.3	63.7	77.6	80.4	82.2
Treatment for neuropathic pain	14.7	4.5	8.3	11.7	23.2	22.5	18.7	16.2	15.0	29.9	11.8	15.0
Any component	97.3	77.5	78.3	92.5	87.2	92.8	100.0	98.1	66.4	85.1	82.4	92.5

Table 10 Percentage of People Ever Receiving Care at the Facility and Elsewhere, by Facility

	A		B		C		D		E		F	
Component of Care	fac	else	fac	else	fac	else	fac	else	fac	else	fac	else
Assessment of pain	91.7	8.3	38.7	11.7	63.3	19.2	83.3	8.3	61.6	24.0	86.5	28.8
Strong opioids	0.0	0.0	0.9	0.0	0.0	0.0	1.7	0.8	13.6	8.0	0.0	0.0
Weak opioids	1.8	1.8	2.7	0.9	0.8	0.8	4.2	0.0	9.6	8.8	0.0	0.0
Non-opioid analgesics	65.1	44.0	32.4	42.3	44.2	35.0	75.0	35.8	68.0	39.2	78.4	39.6
Neuropathic pain tx	11.9	2.8	4.5	0.0	5.0	3.3	6.7	5.0	17.6	6.4	21.6	4.5
	G		H		J		K		L		M	
Component of Care	fac	else	fac	else	fac	else	fac	else	fac	else	fac	else
Assessment of pain	95.3	14.0	47.6	63.8	14.2	37.2	73.8	36.4	52.0	12.7	88.8	3.7
Strong opioids	4.7	0.0	2.9	8.6	0.9	12.4	0.0	0.0	2.0	0.0	0.0	0.0
Weak opioids	11.2	0.9	1.0	8.6	0.9	12.4	0.0	0.0	11.8	2.0	1.9	0.0
Non-opioid analgesics	98.1	15.0	39.0	89.5	21.2	54.0	69.2	32.7	47.1	58.8	80.4	15.0
Neuropathic pain tx	18.7	1.9	10.5	6.7	0.9	14.2	29.9	2.8	9.8	2.9	15.0	0.0

Section 5 Results 2: Combination of Data from the Two Countries

5.1 PHASE 2 QUANTITATIVE COHORT AND PHASE 1 PHARMACY REVIEW

5.1.1 Pain Prevalence Over Time

Figure 6 to Figure 8 below show pain scores over time for the four time points in the study, which were typically one month apart (mean 31.4 days, standard deviation 12.7).

Figure 6 POS 1 Scores Over Time, Reports of Pain

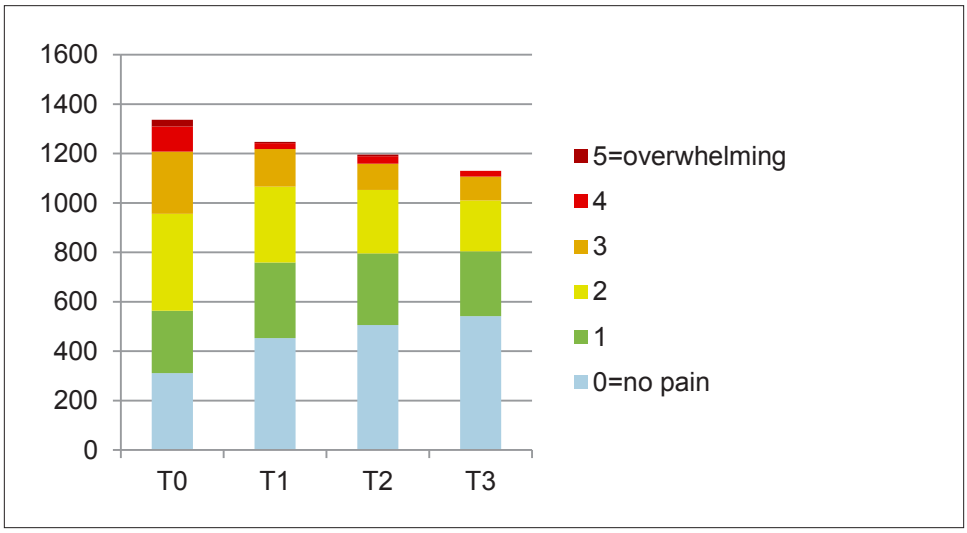
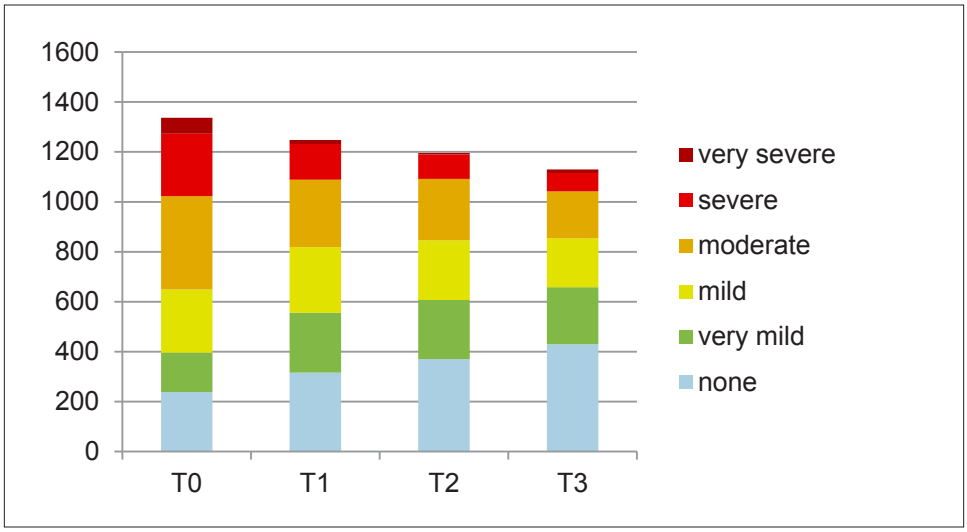


Figure 6 is displayed using the number of participants rather than the percentage in order to demonstrate the contribution of both loss to follow-up and change over time to the results. Of the 1337 recruited, 1130 gave data at all four timepoints (84.5%).The number of people to report no pain increases, as well as the proportion. The number reporting a score of 1 increases slightly while all other scores become less prevalent and no participants report overwhelming pain by T3.

Figure 7 **MOS-HIV 2 Scores Over Time, Reports of Pain**



The results in Figure 7 are similar to those in Figure 6, but scores remain more severe at all time points (demonstrating differences in the measures' sensitivity).

Figure 8 **MOS-HIV 3 Scores Over Time, Pain Interference with Daily Living**

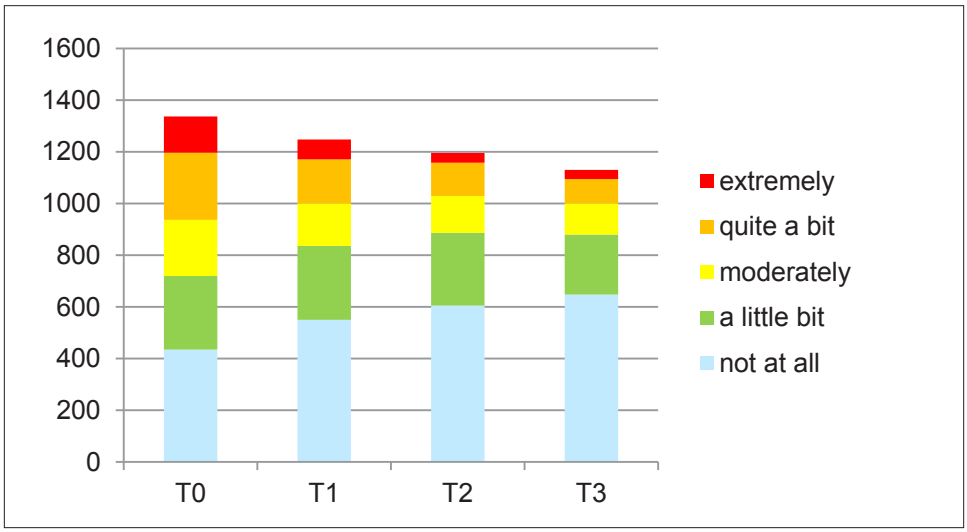


Figure 8 shows that pain causes less interference with daily living over time and by T2 around half of participants reported that pain interfered with their lives.

The graphs show that on average, pain scores improve over time. However, this effect could mask the persistence of severe pain in a small number of people. Score change over time for participants with pain scores of 4 or 5 at baseline is populated in Table 11. At T3, three months later, no participants reported overwhelming pain and the majority (59%) reported pain scores of 0 or 1.

Table 11 Pain APCA African POS Item Scores Over Time for Those Who Experienced the Worst Two Scores at T0

Pain Score	T0	T1	T2	T3
5 (overwhelming pain)	28	0	1	0
4	48	5	2	3
3	0	8	5	7
2	0	24	19	16
1	0	18	13	17
0 (no pain)	0	13	26	20
Total	76	68	66	63

5.2 PHASE 2 QUALITATIVE INTERVIEWS

5.2.1 Description of Sample

There were 83 patient interviews, 47 carer interviews and 59 staff interviews were conducted between 26 February and 13 October 2008, 91 in Uganda and 98 in Kenya, making a total of 189.

There were seven patient interviews from each facility except Facility H which did six, and five staff interviews from each facility except for Facility L which did four. For carer interviews, six facilities did five each, Facility G and L did four, Facility B and E did three, Facility M did two, and Facility J did one. Characteristics of the interviewees are presented in Table 12, Table 13, and Table 14.

Table 12 Patient Characteristics (N = 83)

Characteristic		Kenya (n = 42)	Uganda (n = 41)	Total (n = 83)
Female n (%)		28 (67%)	20 (49%)	48 (58%)
Mean age (range, median)		35 (20–56, 34)	37 (18–61, 37)	36 (18–61, 37)
Receiving ART n (%)		29 (71%)	28 (68%)	57 (69%)
Mean household size (range)		4.7 (1–10)	4.7 (1–10)	5.7 (1–13)
Location	Rural	23	7	30
	Peri-urban	9	18	27
	Urban	9	16	25

Table 13 Care Giver Characteristics (N=47)

Characteristic		Kenya (n = 26)	Uganda (n = 21)	Total (n = 47)
Female n (%)		14 (54%)	14 (67%)	28 (60%)
Mean age (range, median)		40 (20–72, 37)	29 (18–52, 27)	35 (18–72, 32)
Mean household size (range)		5.6 (2–10)	5.6 (2–10)	6 (2–11)
Location	Rural	14	8	22
	Peri-urban	7	7	14
	Urban	5	6	11
Relationship to patient[a]	mother	4	2	6
	father	1	0	1
	sister	1	1	2
	brother	3	4	7
	daughter	2	3	5
	son	2	0	2
	wife	2	6	8
	husband	6	1	7
	aunt	3	1	4
	friend	1	3	4
	cousin	1	0	1

[a] Sometimes these are categorical terms rather than blood relationship, for example the care giver who identified himself as a father explained during the interview that he was actually the patient's uncle.

Table 14 Staff Characteristics (N = 59)

Characteristic		Kenya (n = 30)	Uganda (n = 29)	Total (n = 59)
Designation	clinical officers	4	2	6
	nurses	5	6	11
	counselors	1	8	9
	nurse counselors	2	3	5
	nutritionists	4	0	4
	doctors	2	2	4
	social workers	1	1	2
	medical officers	2	5	7
	lab technologists	1	1	2
	nursing officers	1	1	2
	community nurses/ workers	4	0	4
	others	3	0	3
Mean time working at the facility (range, median)		5 years (2 months to 26 years, 2 years)	5 years (2 months to 24 years, 4 years)	5 years (2 months to 26 years, 3 years)

5.2.2 Participant Identification Codes

P represents an interview with a patient, S a member of staff, and C a family caregiver. Facilities are coded by a letter, A–M, missing out the letter I to avoid confusion with number 1. Facilities A–F are in Kenya, and G, H, J, K, L, and M are in Uganda.

5.2.3 Staff Views on Pain Control

Staff described a need for analgesics:

> "The two or I would say three key drugs which we usually buy but they are never enough for our patients are Pyridoxine, amitriptyline or other tricyclic antidepressants which most of the time is not well supplied. We also need acyclovir because we discovered that it is a very expensive drug and we use it frequently; so most of the time even if we prescribe it, the patients are not able to buy."
>
> — *S3 Fac A*

> "In addition to what we have, it would be good to at times have analgesics; strong analgesics for patients with chronic pain. We do have painkillers, I didn't mention pain killers, general basic analgesics is what we stock, but, at times its good to stock one strong analgesic not for all the patients but for those who do require…Oral analgesics are what we are talking about; morphine or drugs in that category."
>
> — *S1 Fac D*

> "We don't have Morphine but I don't know whether it is possible to have it. I think it would be important to have it because of some patients."
>
> — *S3 Fac E*

> "I think it would be good to get oral morphine for pain management because we get certain patients in severe pain and all we have is codeine phosphate."
>
> — *S1 Fac M*

5.2.4 Patient Description of Pain Experience and Needs, and Family Caregiver Description

The most commonly reported patient physical problem was pain:

> Respondent: "And my chest is painful and uncomfortable; I am coughing and producing very black/dark saliva and thus I am wondering why…I have painful joints and especially when I am sleeping."
> Interviewer: "So you have painful joints?"
> Respondent: "Yes, whenever I lie down, it becomes difficult to rise up."
>
> — *P3 Fac E*

> "My whole body hurts and I spend a lot of time in bed; I have no energy and I am not able to get out of bed."
>
> — *P6 Fac E*

> "Sometimes she has this severe pain in her right leg and some times she applies medicines and it stops but it is recurrent. May be after a month or two weeks or even after a week. Like now she is experiencing the pain and that's why she is not able to walk up here with me and that is why I am here to collect her drugs from this clinic."
>
> — *C1 Fac L*

> "Yes, like the ARVs at times cause me stomach pains and pains in the legs and at times severe headache and rotational dizziness and I feel as if I lose balance and focus."
>
> — *P3 Fac L*

> "What is almost disturbing me is my chest pain. This one is always disturbing me."
>
> — *P4 Fac G*

> "She has been falling sick often, time and again she is down with malaria, fever, diarrhea and general body pain and these days she gets severe pain in the bones and this pain has limited her from doing any other work. There is a lot of pain in the joints, she feels these are the problems she has being HIV positive client and these never used to have them before."
>
> — *C4 Fac G*

Emotional problems were multifaceted—both as a result of living with the knowledge of diagnosis and related to the financial problems experienced as a result of the diagnosis:

> "At times when I start having a lot of thoughts my head throbs."
>
> — *P2 Fac E*

> "The other problem is, you come to town; you try to find a job; you don't get; you go home; you are so troubled; my heart sometimes go down; psychologically, I am so much affected"
>
> — *P2 Fac B*

There could also be health costs for care givers, such as the strain of queuing for hours at the health facility:

> "Whenever I go there I over-stand waiting for the drugs and end up feeling a headache and some backache pain."
>
> — *C2 Fac H*

The secondary analysis reported below in section 4 explore these themes in more detail.

Section 6 Results 3: Secondary Analysis

6.1 IS RECEIPT OF ANALGESIA ASSOCIATED WITH DEMOGRAPHIC OR CLINICAL CHARACTERISTICS?

6.1.1 Opioids

During the study, 114 participants (8.5%) received an opioid; 23 morphine, 49 codeine, and 42 both. Table 15 shows bivariate analysis of association of demographic and clinical variables with ever receiving an opioid analgesic, using random-effects logit models to adjust for facility.

Table 15 Bivariate Multilevel Models of Association of Covariates with Receiving Opioid During Study

Variable		%	OR	p
Gender	Male Female	7.1 9.2	1.30	0.263
Age category	18–29 30–39 40–49 50–59 60–70	8.2 8.4 9.1 9.5 5.9	1.00	0.964
Education	None Began primary Began secondary diploma/ degree	11.4 8.3 8.5 8.1	0.87	0.342
Wealth quintile	Lowest Second Middle Fourth Highest	9.6 7.5 7.1 11.2 7.1	1.00	0.958
Functional status	0 1 2 3 or 4	6.3 10.3 12.8 34.8	1.83	<0.001
Newly diagnosed	Yes No	6.6 9.5	0.69	0.164
Used ART	Yes No	10.4 7.1	1.46	0.106
CD4 count	0–100 101–200 201–350 350+	11.2 9.8 7.5 8.2	0.83	0.077

The two variables associated with receiving an opioid in bivariate analysis at p<0.1 were functional status and CD4 count. Those with limited functional status using the ECOG (i.e., higher the score the lower the functional status) and with a lower CD4 count were more likely to receive opioids during the study. Over a third (34.8%) of those with the lowest category of functional status received opioids. The association with CD4 count had low significance (p = 0.077) and the distribution was not linear, as people with a CD4>350 were slightly more likely to receive an opioid than those with CD4 between 201 and 350. When the two variables were taken forward into a multivariate model, CD4 count dropped out of the model as non-significant, leaving only functional status (OR = 1.83, 95% confidence intervals 1.40–2.38). After adjusting for functional status, opioid use was equally probable regardless of CD4 count.

6.1.2 Non-opioids

During the study, between 63.2% and 100% of participants received a non-opioid analgesic from their care facility, depending on the site. Non-opioid analgesics were more common among older people in general although the oldest group, aged 60–70, did not continue this trend (Table 16). Poorer people and people with limited function (i.e., higher ECOG score) were more likely to receive non-opioids. Those with a new diagnosis and those not taking ART were less likely to receive them.

Table 16 Bivariate Mmultilevel Models of Association of Covariates with Receiving Non-opioid Analgesic During Study

Variable		%	OR	p
Gender	Male Female	80.7 80.5	0.95	0.721
Age category	18-29 30-39 40-49 50-59 60-70	74.6 81.9 86.0 82.4 76.5	1.02	0.009
Education	None Began primary Began secondary diploma/ degree	89.8 80.5 78.6 81.1	1.02	0.867
Wealth quintile	Lowest Second Middle Fourth Highest	88.9 83.1 81.2 78.0 71.1	0.87	0.027
Functional status	0 1 2 3 or 4	75.4 86.5 93.1 95.7	1.87	<0.001

Variable		%	OR	p
Newly diagnosed	Yes No	74.9 83.2	0.74	0.065
Used ART	Yes No	85.7 76.6	1.47	0.025
CD4 count	0-100 101-200 201-350 350+	80.1 86.6 80.5 80.3	0.96	0.633

Age, wealth quintile, functional status, time since diagnosis and ART use were put into a multivariate model. After sequential removal of all covariates associated with less than 95% significance, two were left (Table 17). Older people and people with limited physical function were more likely to receive non-opioid analgesics. Wealth quintile was dropped because the p-value was 0.08.

Table 17 Multilevel Model of Association of Covariates with Receiving Non-opioid Analgesic During Study

	OR	95% CI	Z	P
Age group	1.02	1.00 to 1.04	2.58	0.010
Functional status	1.86	1.42 to 2.44	4.48	<0.001

6.1.3 Neuropathic

During the study, 0.9–29.9% of participants received treatment for neuropathic pain at their care facility, depending on their providing site. Treatment for neuropathic pain was closely associated with age, becoming more common as age increased, with the exception of the group aged 60–70 who rarely received neuropathic pain treatment (Table 18). There was a clear trend for poorer people and those with lower functional status to be more likely to receive treatment. Newly diagnosed people were less likely to receive it. Those with CD4 count below 100 were the least likely to receive treatment for neuropathic pain but there was no consistent relationship between treatment and CD4 count.

Table 18 Bivariate Multilevel Models of Association of Covariates with Receiving Treatment for Neuropathic Pain During Study

Variable		%	OR	p
Gender	Male Female	18.2 14.9	0.82	0.206
Age category	18–29 30–39 40–49 50–59 60–70	11.5 15.4 20.3 28.4 11.8	1.03	<0.001

Variable		%	OR	p
Education	None Began primary Began secondary diploma/ degree	17.1 15.4 15.1 21.6	1.09	0.388
Wealth quintile	Lowest Second Middle Fourth Highest	18.9 18.0 16.2 14.6 12.0	0.86	0.022
Functional status	0 1 2 3 or 4	12.8 19.4 22.6 34.8	1.50	<0.001
Newly diagnosed	Yes No	11.4 18.1	0.58	0.004
Used ART	Yes No	17.0 15.0	1.28	0.151
CD4 count	0–100 101–200 201–350 350+	12.4 15.0 19.5 14.6	1.05	0.594

Age, wealth quintile, functional status and time since diagnosis were taken forward into multivariate analysis. Wealth quintile became non-significant and was dropped, leaving the model in Table 19. Older people (with the exception of those over 60, as seen in Table 18), those with impaired physical function, and those with a previous HIV diagnosis were more likely to have treatment for neuropathic pain during the study. Functional status had the biggest effect of the three.

Table 19 Multilevel Model of Association of Covariates with Receiving Treatment for Neuropathic Pain During Study

	OR	95% CI	Z	P
Age group	1.03	1.01 to 1.05	3.79	<0.001
Functional status	1.47	1.20 to 1.81	3.64	<0.001
Newly diagnosed	0.62	0.43 to 0.91	–2.48	0.013

6.2 HOW DOES PAIN SELF-REPORT CHANGE OVER TIME?

A combined pain score was created from the three pain items as described in the methods.

Table 20 shows that over time, the proportion reporting severe pain reduced a lot, the proportion reporting moderate pain reduced a little and the proportion reporting mild pain increased to more than half (51.9%).

Table 20 Combined Pain Score by Time Point

Combined pain score	Time point			
	T0	T1	T2	T3
Low	22.4	34.9	43.4	51.9
Moderate	40.2	36.7	36.5	31.6
Severe	37.4	28.4	20.1	16.5

An important finding from this study is that, at any time in the study, 687 participants (51.4%) reported severe pain on at least one of the three outcome variables.

The proportion reporting severe pain on at least one variable by facility is shown in Table 18. 'Severe pain' is defined as a score of 4 or 5 on the POS pain item, 5 or 6 on MOS-HIV question 2, or 4 or 5 on MOS-HIV question 3. At seven facilities, the proportion reporting severe pain was within six points of the average for the sample (i.e., 45.6% to 57.0%). Facilities J, K and L had a lower period prevalence of pain, at about a third (30.4% to 34.2%). Facilities G and H had much higher pain prevalence, especially Facility G, where 84.1% of participants reported severe pain at least once.

Table 21 Period Prevalence of Maximum Combined Pain Score at Any Time byFacility (%)

	A	B	C	D	E	F	G	H	J	K	L	M
Severe combined pain score	48.6	34.2	50.0	55.0	45.6	56.8	84.1	70.5	32.7	53.3	30.4	57.0

6.3 IS THE RECEIPT OF ANALGESIA ASSOCIATED WITH REDUCTION IN PAIN SCORES OR IMPROVEMENT IN QUALITY OF LIFE OVER TIME?

Maximum combined pain score (the worst pain score reported at any time point per person) was tabulated against receipt of pain management at any time and chi2 tests were used to examine the association (Table 22). As noted above, pain is very highly prevalent over a four-month period, with over half (51%) of HIV outpatients experiencing severe pain during that time.

It is also very notable that although Figures 6–8 show the majority of people reported low pain at any given time, only 11% (136/1337) reported consistently low pain.

Table 22 Maximum Combined Pain Score by Pain Management

Component of Care	Maximum Pain Score			Chi2	p
	Mild n = 136	Moderate n = 514	Severe n = 687		
Pain assessment	41.2	72.4	85.4	127.4	<0.001
Non-opioid analgesic	44.9	77.6	89.7	149.43	<0.001
Weak opioid	1.5	4.7	9.5	17.44	<0.001
Strong opioid	1.5	3.9	6.3	7.33	0.026
Neuropathic pain treatment	3.7	11.1	22.0	43.01	<0.001

Table 22 above shows that 14.6% of people who had severe pain were never assessed during the four months of the study, and 10.3% did not even receive a non-opioid analgesic which is the first step on the WHO Pain Ladder. Only 9.5% received a weak opioid, 6.3% a strong opioid, and 22% treatment for neuropathic pain. All pain management is correspondingly less common for those whose worst pain score is moderate or who had mild/no pain throughout the study, and these associations are statistically significant. People who reported more pain were more likely to have treatment.

The results of longitudinal mixed-effects logistic regression to show the association of analgesia with pain scores over time are shown in Table 23. Receiving an opioid, non-opioid or neuropathic pain treatment is associated with higher odds of pain over time, even after adjusting for pain score at baseline.

Table 23 Mixed-Effects Logistic Regression Model of Combined Pain Score Over Time and Analgesia

Component of Care	OR	95% CI of OR	Z	p
Baseline combined pain	4.69	3.56–6.19	10.99	<0.001
Opioid	4.13	2.12–8.06	4.16	<0.001
Non-opioid	2.91	2.32–3.67	9.15	<0.001
Neuropathic	1.58	1.04–2.40	2.14	0.032

Combined pain scores by time point were compared between those who had and had not received pain management therapies, to observe whether change in pain score was different between the two groups. Table 24 shows that in the group who received opioids, prevalence of severe pain fell from 52.6% to 27.6% over three months, while prevalence of moderate pain only changed by three percentage points. In the group without opioids, severe pain prevalence more than halved and moderate pain prevalence also fell by nine points.

The prevalence of severe pain was much higher at baseline for those who received non-opioid analgesia than for those who never did, and it rapidly dropped to 29.4% at T1 and finally to 18.4%. The prevalence of moderate pain reduced by six points. In the group who never received a non-opioid, prevalence of severe

pain fell more and prevalence of moderate pain halved. Similarly in the results for neuropathic pain care, prevalence of severe pain fell by around half in both groups but only the group without pain relief also showed reduction in moderate pain.

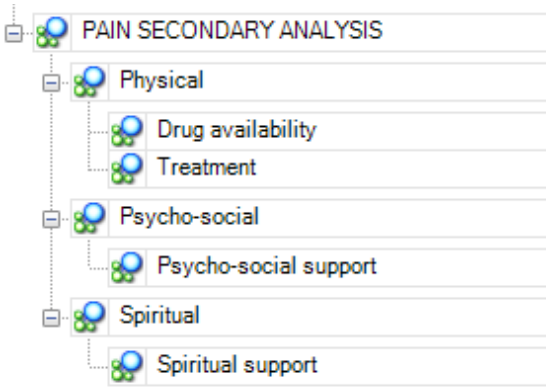
Table 24 Combined Pain Score by Time Point and Receipt of Pain Therapy, %

Component of Care			T0	T1	T2	T3
Ever received opioid	Yes (n=114)	Moderate Severe	39.5 52.6	36.8 43.9	38.9 27.8	36.2 27.6
	No (n=1223)	Moderate Severe	40.3 36.0	36.7 26.9	36.3 19.3	31.1 15.4
Ever received non-opioid	Yes (n=1075)	Moderate Severe	40.4 41.7	39.8 29.4	38.7 22.1	33.9 18.4
	No (n=262)	Moderate Severe	39.5 19.5	23.8 24.2	25.6 9.9	19.7 6.4
Ever received neuropathic	Yes (n=213)	Moderate Severe	35.2 51.2	44.6 35.2	37.2 29.0	35.3 23.4
	No (n=1124)	Moderate Severe	41.2 34.8	35.2 27.1	36.4 18.2	30.8 15.0

6.4 WHAT ARE THE THEMES CONNECTED TO EXPERIENCES OF PAIN AND PAIN MANAGEMENT FOR HIV PATIENTS, FAMILY MEMBERS, AND STAFF?

Secondary analysis of the qualitative data related to pain resulted in the coding frame in Figure 9.

Figure 9 Coding Frame for Secondary Analysis of Qualitative Pain Data



Central to the theme of pain was its multi-dimensional nature: pain was not just physical, but also psychological, social and spiritual. Psychological and social aspects of pain were strong themes which were closely related; the psychosocial theme encompasses both. Themes connected to experiences of pain and pain management are discussed in turn by interviewee category.

6.4.1 Patients

Physical Pain

Patients discussed experiences of physical pain caused by their illness as well as by co-morbidities:

> "The worst thing now is the pain in the knee. This pain is severe and it is making me not eat. I also have pain in the chest which is due to the chronic asthma, although I am in hospital often for treatment it seems I am not responding very well. I feel bad but I am managing with the help of ARVs and without ARVs I would probably be dead by now."
>
> *— P7 Fac G, female, age 35, on ART, urban area, Uganda*

> "My whole body hurts and I spend a lot of time in bed; I have no energy and I am not able to get out of bed."
>
> *— P6 Fac E, female, not on ART, urban area, Kenya*

> "And my chest is painful and uncomfortable; I am coughing and producing very black/dark saliva and thus I am wondering why... [And] I have painful joints and especially when I am sleeping... whenever I lie down, it becomes difficult to rise up."
>
> *— P3 Fac E, male, age 38, not on ART, rural area, Kenya*

> "I do not have energy. Sometimes I get diarrhoea, sometimes I feel nausea, this time it came in form of cough and chest pain."
>
> *— P4 Fac F, female, age 22, not on ART, rural area, Kenya*

> "What happened is that in the year 2004 in the morning of Dec 24th, my stomach started paining very hard and I told my wife that there is a problem. On that day, we were meant to go on safari together with the children and I just asked them to proceed as I stayed home to observe my status and go the hospital later. But the pain got so severe that my wife decided that we should instead use the vehicle that was intended to take us on safari to go and collect medicine."
>
> *— P4 Fac E, male, age 47, on ART, rural area, Kenya*

This patient and others also described the symptoms associated with neuropathic pain:

> "Now I only have some little pain at the bottom of my foot but this pain is not so much because it does not interfere with my work; it makes me feel like I have stayed in cold water for a long time; it's just that."
>
> *— P4 Fac E, male, age 47, on ART, rural area, Kenya*

Patients also described pain as a side-effect of treatment:

> "If you take these medicines without eating, you are going to suffer."
>
> *— P4 Fac D, male, age 27, on ART, urban area, Kenya*

"One day my leg was paining very much from down there to the knees; then I reported to a nurse here; and the doctor told me that there is this capsules that I take; I think it is called Stavudine; he told me that this medicine has side effects sometimes. The doctor then told me, 'We have to change that Stavudine and then we replace it with another drug.' After they had removed that drug from my list, the pains went away."

— P4 Fac E, male, age 47, on ART, rural area, Kenya

"There is some medicine that I take in the evenings, it is yellowish in colour, it makes me sleepy and sometimes it gives me a headache; and when I am waking up it is a bit difficult and even if my child is crying at night, I have a problem waking up to attend to him."

— P7 Fac E, female, age 34, on ART, urban area, Kenya

For some patients, the experience of pain was associated with finding out they had HIV infection:

"I came to know about this place at a time when I was admitted in the ward during the same time when I lost my eyesight. At that time, I had a both my head and neck were in pain and they extracted some fluid from my spinal cord and when I came to; I saw darkness. Before then I had a wound which did not last for long. The doctor who had extracted the fluid from me told me; 'X, do you know you have HIV?'"

— P5 Fac B, female, age 44, on ART, rural area, Kenya

Patients did not always report the pain they experienced to healthcare staff:

"In fact I don't complain about these problems such take an example of this problem with my legs, I haven't complained about it because I realized that they were not painful as a whole but I mostly experience pains in the joint."

— P4 Fac L, female, age 42, on ART, urban area, Uganda

Patients described the benefit of receiving pain treatment through the facilities:

"They give me drugs like dichlofenac, drugs like Amoxylin, capsules and some of other drugs which I have forgotten but most given when you have severe pain."

— P4 Fac G, male, age 46, on ART, rural area, Uganda

One patient mentioned the complementary therapies available through some facilities

"They give this when they do not want to give you drugs, sometimes when you feel pain in the joints, when you have muscle pains or else when you have the herpes zoster, they just prescribe you to go to the aroma therapy and then you get that treatment of aroma which is given using the hands or massage. Then another treatment...no, those are the ones."

— P1 Fac H, female, age 40, on ART, urban area, Uganda

Psychosocial Pain

Patients described the pain caused by stigma:

> "Some people in community look down at you, they see you as nothing. Sometimes if you are working they just discriminate and sometimes they stigmatise you and you feel like you are nothing. You feel like you should stop working…I feel like stigma and discrimination is the most pressing problem we face."
>
> *— P1 Fac H, female, age 40, on ART, urban area, Uganda*

> "I don't know whether it's because people are still illiterate or they just don't understand but they are very malicious. Now we people who are affected with this HIV virus, our neighbors, our friends, some of our relatives take no interest in whatever we are doing [or] else their wishes are we must all die. Not even appreciating you inside his house to share some meals with you, not even accepting your ideas, not even respecting you as somebody alive."
>
> *— P2 Fac H, male, age 40, not on ART, peri-urban area, Uganda*

> "One neighbour commented recently, 'I am surprised this lame woman contracted HIV, do they also engage in sex? Funny!' Others keep reckoning, 'That one has a soil notice, she is a moving grave…You go in for her, be ready for death.'"
>
> *— P1 Fac L, male, age 37, on ART, urban area, Uganda*

Patients described feeling lonely and isolated:

> "Loneliness, sometimes I am just alone in the house…it is terrible for me these days and worst when children return to school. At times you can fall sick and there is no one to even offer you a glass of drinking water."
>
> *— P1 Fac L, male, age 37, on ART, urban area, Uganda*

> "What I see important in my life is having a confidant [with] whom to share the inner most feelings and problems, because there are some problems you can't just tell anyone because we as human beings were are nurtured differently, and there some persons you can't trust with words but there are those [with] whom you can share. But to me, I have no such friend I can trust with the innermost word. I don't have that person at all."
>
> *— P3 Fac L, male, age 36, on ART, urban area, Uganda*

The suffering and 'psychological torture' (P6 Fac L) caused by poverty was another strong theme:

> "Sometimes you cannot afford to buy food to eat at times you cannot sustain yourself completely. At times you cannot afford transport costs to come for treatment. And again with these drugs we take, one must feed well and because you cannot really work hard enough because of compromised health at times even getting this food is a big problem. So you may have to stop the drugs because they really raise your appetite. Those are the major challenges."
>
> *— P1 Fac L, male, age 37, on ART, urban area, Uganda*

"The problem I have [is that] I lost my husband when I was still young. I had only three children but the last one also followed his father [died], now I have only two girls. One is in primary seven, another one in primary four, but I am failing to look after them because he left me with nothing... I don't know whether that one who is in P7 will start senior one because no money, no land. I don't have anything."

— P7 Fac M, female, age 23, on ART, urban area, Uganda

Interviewer: "What would you say are your biggest problems ever since you were diagnosed with the virus?"
Respondent: [Almost breaks down]. "The problem that I have had is that of food. I used to live with my sister and I don't get along with her. When she heard that I have the HIV virus, she chased me away. I now live with other ladies, and I don't work." [Starts to cry]

— P3 Fac D, female, age 24, on ART, peri-urban area, Kenya

Social and psychological problems were not necessarily shared with healthcare staff:

"I have never done so because none of them has ever asked me about that. However, if they had asked I would have explained as I have done it to you."

— P5 Fac H, male, age 38, not on ART, urban area

Interviewer: "Are there any other problems that you have and have not been able to talk about them with the HCWs?"
Respondent: "Other problems include where we live; both the roof and walls of those houses are made of corrugated iron sheets and the floor is made of earth. With the cold Kericho weather, the problem of beddings is quite real to me and we buy beddings for ourselves; and because I do not have a lot of money; I can only buy the blanket that costs Kshs 200 and this is very light; and if I wanted to buy a blanket that would protect me from cold, you find this would cost me Kshs 1000 plus."

— P1 Fac E, male, age 40, on ART, urban area, Kenya

Patients who had acquired HIV at a young age and before fulfilling their dreams were particularly susceptible to psychological pain:

"One thing that has really brought grief and pain to me is that I acquired HIV at an early age before even having a child that is what hurts me."

— P3 Fac K

Difficult family relationships were also reported as a cause of problems:

"There are times when I get some problems especially in my home. My in laws disturb me a lot. Am planning something so that we have a bright future because we are sick (yet for them are okay) but my in laws are a pain. They come and cause misunderstandings between me and my husband were by we fail to agree on some issues. This hurts me a lot."

— P4 Fac K, female, age 26, not on ART, peri-urban area, Uganda

"[I have] two wives, one can understand and the other one cannot understand the situation. So whenever we are together we don't rhyme, it is just a matter of quarrelling…There are so many things with HIV, as we are three adults in the family; you cannot know who brought the disease, so this one is complaining, this one is complaining, this one is complaining, nobody is accepts that 'I am the person who terminated everybody in the family', so it is a quarrel. This one blames the other, this one blames the other."

— P1 Fac A, male, age 49, not on ART, peri-urban area, Kenya

Spiritual Pain

Patients described spiritual pain and despair:

"My biggest worry is about my future. I have no child and my dreams are shuttered down and it hurts lots. It is an inner most pain which I can't explain to anybody and when you see people who have died because of this disease and yet they have been on ARVs and yet they die mysteriously, I feel weighed down and lose hope most often."

— P3 Fac L, male, age 36, on ART, urban area, Uganda

"The other problem is, you come to town, you try to find a job, you don't get [one], you go home, you are so troubled... My heart sometimes go[es] down. Psychologically, I am so much affected and even sometimes I was asking, 'If God, you knew this, why wouldn't you just take me so that these things can come to an end?' But He has not done so, I am still alive."

— P2 Fac B, male, age 53, on ART, peri-urban area, Kenya

Illness was often experienced through a spiritual lens:

"I was given nutritional education then I started taking my medication, but after some time I started getting serious drug side effects [interviewee breaks down in tears]. I could not overcome the drug side effects, and I was tempted to stop probably by an evil spirit. But with prayers I continued taking the drugs."

— P7 Fac G

While the supportive role of spiritual practices and beliefs was a major theme, problems related to illness could have an impact on patients' spiritual lives:

"I always go to church and pray. But still I worry a lot because I have many things that disturb me. I always think about my young child who is sick, she is mental[ly ill] yet I am the only person taking care of her…So even when you go pray you get those flash backs about the child."

— P4 Fac K, female, age 56, on ART, peri-urban area, Uganda

One patient described the spiritual counselling received from the facility's healthcare workers:

> "We are encouraged to put our trust in God: He can give life, so it may not even be HIV [that] kill[s] you; one['s] death is always decided by God, so death should never worry us."
>
> *— P1 Fac M, male, age 39, not on ART, rural area, Uganda*

6.4.2 Family Care Givers

Physical Pain

Family care givers reiterated that patients experienced debilitating physical pain associated with HIV and its treatment:

> "She has been falling sick often, time and again she is down with malaria, fever, diarrhea and general body pain and these days she gets severe pain in the bones and this pain has limited her from doing any other work. There is a lot of pain in the joints, she feels these are the problems she has being HIV positive client and these never used to have them before."
>
> *— C4 Fac G, female, age 40, friend, peri-urban area, Uganda*

> "She has been using the ARVs but she has not been doing well. When she started taking the medications, she felt better, but later she started having back pains. X-ray was taken and sputum examination was also done. She was then given some medications for the back pain."
>
> *— C1 Fac A, male, age 60, husband, rural area, Kenya*

> "The only problem that she has is the pain in her kidneys. She feels pain when she stands up and when she bends. If she didn't have that pain, she would be very much okay."
>
> *— C4 Fac D, female, age 38, daughter, peri-urban area, Kenya*

Again, care givers suggested that not all physical pain is reported by patients:

> Respondent: "Sometimes she has this severe pain in her right leg and sometimes she applies medicines and it stops but it is recurrent."
> Interviewer: "How often does she experience this pain in her leg?"
> Respondent: "May be after a month or two weeks or even after a week. Like now she is experiencing the pain and that's why she is not able to walk up here with me and that is why I am here to collect her drugs from this clinic."
> Interviewer: "When she experiences this kind of pain in her legs, does she come to report the pain to the health workers at this facility?"
> Respondent: "For sure, I don't think she reports it the health care workers here."
> Interviewer: "Could you know the reasons why she doesn't report the pain to them?"
> Respondent: "I don't know, sir."
>
> *— C1 Fac L, female, age 19, daughter, urban area, Uganda*

Care givers themselves experienced physical pain caused by their caring role:

> "Whenever I go there [to collect the drugs] I over-stand waiting for the drugs and end up feeling a headache and some backache pain."
>
> *— C2 Fac H, female, age 28, wife, urban area, Uganda*

Psychosocial Pain

Care givers as well as patients described social stigma as highly prevalent and detrimental:

> "What hurts me is the way other people look at us - they say that my husband was a proud man so now it is his time to face the problems, so when I hear those words I feel so hurt." [Care giver broke down in tears]
>
> *— C1 Fac H, female, age 35, wife, urban area, Uganda*

> "There is stress and stigma, you find this in the community like our neighbours peep at us to see they say there is no family there they are all going to die so we have that stigma."
>
> *— C5 Fac H, male, age 26, brother, rural area, Uganda*

Care givers described the pain experienced by patients who become socially isolated and hopeless owing to their HIV diagnosis:

> "Usually you find that these patients have withdrawn away from the community and their close people. They just stay alone and give up and lose hope in life and also feel that they have already gone to the end of life. They have a thinking that AIDS has marked the end of their life and because of this negative thinking towards life usually they don't come for medication."
>
> *— C2 Fac G, male, age 24, brother, urban area, Uganda*

> "When [my mother] went back to stay with my sisters-in-law, they found out her status and it's from that moment that they started behaving like they don't want her. If she wanted to help them with the grandchildren, they didn't want that…they would tell her off. So my mother was always in a sad mood, always holding her cheek. She was really hurt. I was also hurt since I could not go back to the home where I was brought up in and when I requested my mother to come and stay with me, she would say no."
>
> *— C4 Fac D, female, age 38, daughter, peri-urban area, Kenya*

Care givers themselves suffered psychologically and socially, particularly when the patient was the primary breadwinner:

> "Since he became ill he no longer works although he gets the salary it is not enough. We have many children, mine are two and his are about seven so the challenge I have is school fees and the feeding."
>
> *— C1 Fac H, female, age 35, wife, urban area, Uganda*

> "I only know about one problem and it is about money. Like she is no longer gainfully employed as she was before. Sometimes she doesn't get the money yet she has to feed us and so on. Like at times she delays to meet our school fees."
>
> *— C1 Fac L, female, age 19, daughter, urban area, Uganda*

Ensuring the patient received the care and nutrition required also placed a direct strain of care givers, as described by the same patient in Uganda:

> "Even transport to the facility, because of his condition we need fuel to go the facility because we must use a vehicle. I do not have enough money to feed him so I usually struggle so much, inside my heart I feel he is not feeding properly because I cannot afford the food, I do not have enough money."
>
> *— C1 Fac H, female, age 35, wife, urban area, Uganda*

The time taken caring for patients impacted on the time care givers have available to work, contributing to the socio-economic burden:

> "Most of the time I am caring for the patient so I no longer carry out any casual labour to earn some money."
>
> *— C4 Fac H, female, age missing, wife, rural area, Uganda*

This was of course especially problematic when more than one family member was infected:

> "We have three positive people in the family and they need food. Two of them are ARVs and for me I have to work and at the same time monitor the other clients in the house and they also need food so it is a challenge."
>
> *— 255 Fac H, male, age 26, brother, rural area, Uganda*

Spiritual Pain

Care givers described how the practical consequences of illness could have spiritual implications for patients:

> "Well, once in a while they may ask him why is not going for prayers, but for him, he may be having a skin a rash so he cannot go to church for people to look at him and stigmatise him. What would he go to there for? So there is that problem of stigma and stress, it affects him and he cannot just go out freely. This is a big challenge for men: once he sees his skin has a rash, he has lost his hair, they tend not to want to join other groups or even go church for prayers."
>
> *— C5 Fac H, male, age 26, brother, rural area, Uganda*

6.4.3 Staff

Treating physical pain

Staff reported that pain control was more challenging in patients with advanced disease, in part due to lack of appropriate drugs:

> "But such a person may be difficult to deal with even concerning with the drugs, because it depends on the type of health centre were you are working because you might not have some particular drugs which may make the patients suffer more with pain and all that."
>
> *— S4 Fac J, Counsellor, 2 years' experience, Uganda*

Staff gave mixed reports about the availability of pain-relieving drugs:

> Interviewer: "Are there problems that patients come with to your facility that you are unable to handle? Something like pain, severe pain, depression."
> Respondent: "I can say that I haven't come across any with severe pain that is not controlled. Probably it's because very few have been in the AIDS stage here in this clinic. At least we have the drugs that can control pain up to pethidine. The oral ones, may be like morphine are available but under prescription strictly. Those can be available but only in the inpatient."
>
> *— S5 Fac C, Doctor, 3 years' experience, Kenya*

> "What we don't have is pain relief, we do not have strong opioids like morphine but have Efidine but use weak opioids like Ibrufene, dichlofenac both injection we have them but some strong opioids like morphine syrup we don't have but we have pethedine injection."
>
> *— S1 Fac G, Nurse counsellor, 24 years' experience, Uganda*

> "For severe pain I don't know what drugs they have, I don't know whether they have codeine and those other drugs which they give clients who have those extensive pains."
>
> *— S1 Fac J, Counsellor, 10 years' experience, Uganda*

Use of the WHO pain ladder approach was described:

> "We are trained in palliative care, we have a palliative care nurse and I think when someone is in severe pain the way you have called it then we consider morphine. She was trained and she usually gets the morphine and takes to the clients. But usually there is that severe pain they start with the usual pain killers like panadol, indocid if the pain refuses to go then she results to morphine."
>
> *— S5 Fac H, Nurse, 4 years' experience, Uganda*

Where facilities did not have access to strong pain medication, this was usually recognised as a need:

> "I think it would be good to get oral morphine for pain management because we get certain patients in severe pain and all we have is codeine phosphate. It would also be nice to have chepharosporins because we have people who get severe bacterial infections and it would be nice to put them on something that is more effective."
>
> *— S1 Fac M Clinical officer, 9 months' experience, Uganda*

> "In addition to what we have, it would be good to at times have analgesics; Strong analgesics for patients with chronic pain. We do have painkillers, I didn't mention pain killers, general basic analgesics are what we stock, but at times it's good to stock one strong analgesic not for all the patients but for those who do require."
>
> *— S1 Fac D, Medical officer, 1 year experience, Kenya*

However, this was not always the case:

> Interviewer: "Is pain managed well?"
> Respondent: "Yes"
> Interviewer: "What medicines do you use for pain?"
> Respondent: "We have brufen"
> Interviewer: "What about cases of severe pain?"
> Respondent: "We don't have any other except brufen."
>
> *— S6 Fac A, Nurse counsellor, 6 years' experience, Kenya*

Staff at some services described training initiatives that had been implemented with respect to the management of physical pain:

> "First of all what we did was having a training for some of our staff on management of pain. This was conducted by Hospice Africa Uganda and we had clinical officer, nurses etc. we tried to follow them and monitor on this treatment of pain in a larger manner. We got even things up to Codeine, Morphine for management of severe pain."
>
> *— S5 Fac G, Medical superintendent, 5 years' experience, Uganda*

Staff in Uganda also described collaboration with and referral to hospice:

> Respondent: "Severe pain we try to manage with these common pain killers but we cannot go to the extent of, like, Hospice."
> Interviewer: "So how do you handle that?"
> Respondent: "We refer."
>
> *— S4 Fac H, Counsellor, 3 years' experience, Uganda*

> "[For] severe pain, as I told you we work with Hospice Africa, sometimes they pay visits to us here when there is a pain they can't manage. We contact them and write referral letters and they come and visit our patients here."
>
> *— S2 Fac L, Nurse, 8 years' experience, Uganda*

Responding to Psychosocial Pain

Staff discussed the psychological difficulties facing patients and the counselling offered to alleviate these problems:

> "For most of the patients, disclosure is a problem, because most of them if you ask them if they have disclosed to their family, they say no. most of them fear; like the ones who are married, they fear disclosing to their families, because they fear that somebody can leave her. They also ask about their children; if they are tested and their children are positive. Its like stigma is a lot to them. We do counselling continuously; everyday that we see them, we encourage them; counselling so that at least they can be free to talk to anybody about their status."
>
> *— S5 Fac D, Counsellor, 13 years' experience, Kenya*

Responding to Spiritual Pain

One member of staff described praying with patients and how spiritual solace could help patients in pain:

> Respondent: "Everybody who comes as a patient, we ask them—we don't force them to pray - we ask them, 'Do you want me to pray with you?' If they want to pray with you, you get a scripture then you pray."
> …
> Interviewer: "What about for those in pain, what is the favourite scripture?"
> Respondent: "Well, John 14: 1. The God says I will not let your hearts be troubled—it's a powerful passage. This is the scripture that we use most."
>
> *— S5 Fac M, Social worker, 4 years' experience, Uganda*

A member of staff at another facility described collaborating with local faith leaders:

> Respondent: "We just assist them until their last breath"
> Interviewer: "How do you assist them?"
> Respondent: "We can ask their spiritual leader or the pastor to come and pray for the patient."
>
> *— S6 Fac A, Nurse counsellor, 6 years' experience, Kenya*

However, spiritual care was also recognised to be lacking in the services provided by the facilities:

> "We also have not been able to offer any spiritual care and not that there is lack of personnel and willingness, but it's simply because there is lack of space."
>
> *— S1 Fac E, Doctor, 16 years' experience, Kenya*

Staff also described the spiritual impact or burden that their work could have on them:

> "Spiritually speaking, it is really painful and a very hurting experience. Why? Because there is not much you are going to do. Someone is in your hands, they are trusting you to help, probably do a miracle, but you most times believe this person is not coming up [improving]. I have an experience of a client who we lost this week, she died on Tuesday and for about three months, she was in and out of admission, she had been on first line [ART], she was taken to second line, but you could see she was not improving. It is very bad."
>
> *— S1 Fac M, Clinical officer, 9 months' experience, Uganda*

6.4.4 Summary of the Qualitative Findings on Pain

Findings from the qualitative data revealed the multidimensional nature of pain, which can include psychosocial and spiritual components or manifestations as well as physical. Physical pain was caused by the illness itself as well as treatment side-effects. Care givers reiterated the ways in which HIV and its treatment caused pain. Staff gave mixed reports about the availability of pain relieving drugs, suggesting a large degree of variability between the sites and a lack of access to strong pain relief such as opioids. Pain control was reported to be especially challenging in patients with advanced disease. Facilities in Uganda reported useful collaboration with and referral to Hospice Africa Uganda.

Stigma and poverty were primary contributors to psychosocial pain and appeared highly prevalent. Patients and care givers described how stigma led to isolation, loneliness and hopelessness. Poverty manifested in worries regarding having enough food to eat and having money to pay for transport to the facilities to collect treatment or for children's education. Having acquired HIV at a young age and having difficult family relationships contributed to patients' psychosocial suffering. Patients also described spiritual pain and despair and the impact of illness on their spiritual lives. However, psychosocial and spiritual support appeared to be rarely offered through the facilities. The impact of working in the field of HIV care was also described by staff, evidence of the the need to support staff in order to prevent burn-out.

Findings from the care giver data highlighted the burden of HIV on the family and primary care giver. Care givers reported their own physical and psychosocial pain. Care givers suffered psychologically and socially, especially when the patient was the primary breadwinner in the family. Everyday needs such as food and transport were causes of significant stress, and the time spent caring reduced the amount of time available to earn a living. These problems were exacerbated in situations where more than one family member was infected with HIV.

A particularly important finding in the context of service delivery is that patients do not always report the pain they experienced, whether physical or psychosocial in nature, to healthcare staff. This suggests that eliciting patients' reports of pain in clinical practice may require in-depth probing and communication skills training.

6.5 IS PAIN PREVALENCE ASSOCIATED WITH DEMOGRAPHIC OR CLINICAL CHARACTERISTICS?

Pain prevalence was represented with maximum combined pain score as a binary variable. Participants who at any time during the study reported severe pain on any of the three outcomes were compared with those who never did. Education, wealth quintile, functional status and CD4 count were associated with the odds of severe pain during the study (Table 25). Poorer, less educated people with impaired physical function and low CD4 count were more likely to have pain. Half of those with a CD4 <100, over half of those in the lowest wealth quintile, and over 90% of people with ECOG scores of 3 or 4 reported severe pain at some point during the study.

Table 25 Bivariate Multilevel Models of Association of Covariates with Maximum Combined Pain Score During Study

Variable		%	OR	p
Gender	Male Female	38.9 36.7	0.91	0.443
Age category	18–29 30–39 40–49 50–59 60–70	36.9 37.9 38.1 33.8 41.2	1.00	0.956
Education	None Began primary Began secondary diploma/ degree	50.0 38.7 34.3 31.5	0.80	0.004
Wealth quintile	Lowest second Middle Fourth Highest	52.9 41.2 35.3 29.5 27.4	0.76	<0.001
Functional status	0 1 2 3 or 4	25.6 46.8 80.4 91.3	3.00	<0.001
Newly diagnosed	Yes No	35.8 38.2	0.91	0.413
Used ART	Yes No	39.7 35.5	1.19	0.123
CD4 count	0–100 101–200 201–350 350+	50.9 37.1 34.0 32.7	0.80	<0.001

In multivariate analysis, education and CD4 count were no longer significantly associated with the outcome. People with impaired physical function had a much higher probability of severe pain, and poorer people had higher odds of pain but the effect was less strong.

Table 26 Multilevel Model of Association of Covariates with Severe Combined Pain Score at Any Time During Study

	OR	95% CI	Z	P
Wealth quintile	0.80	0.74-0.88	–4.95	<0.001
Functional status	2.86	2.38-3.43	11.32	<0.001

6.6 IS PAIN SELF-REPORT ASSOCIATED WITH PHYSICAL AND MENTAL QUALITY OF LIFE OVER TIME?

At baseline, POS pain score is significantly associated ($p < 0.001$) with both mental health score ($F = 48.87$) and physical health score ($F = 117.56$). Table 27 shows a clear trend for mean mental and physical health to decline as pain severity increases, and in many cases the 95% confidence intervals do not overlap. Both mental and physical health are lowest when POS score is 4, rather than the maximum 5. However, the number of people reporting 5 is small (n = 27) and so the confidence intervals are correspondingly wider.

Table 27 Relationship Between POS Pain Score and Physical/Mental Health Scores

		Mental health score		Physical health score	
	n	Mean	95% CIs	Mean	95% CI
0=no pain	311	50.9	49.9 to 51.9	52.9	51.8 to 54.0
1	253	49.0	48.0 to 50.0	49.3	48.2 to 50.4
2	392	45.7	44.8 to 46.6	44.4	43.4 to 45.4
3	252	41.8	40.7 to 42.9	36.7	35.5 to 37.9
4	102	39.0	37.1 to 40.8	34.2	32.2 to 36.3
5=overwhelming	27	43.1	38.1 to 48.0	35.1	31.4 to 38.9

Using ANOVA for continuous covariates, both mental and physical health were associated with MOS-HIV pain over the past 30 days (mental health $F = 297.8$, physical health $F = 1316.2$, both $p < 0.001$). Table 28 shows that participants who reported more severe pain had poorer mental and physical quality of life.

Table 28 M2

	n	Mental health score		Physical health score	
		Mean	95% CI	Mean	95% CI
None	238	52.1	51.0 to 53.2	56.4	55.6 to 57.2
Very mild	158	50.4	49.1 to 51.7	51.9	50.7 to 53.1
Mild	253	47.7	46.6 to 48.7	48.7	47.8 to 49.7
Moderate	374	45.0	44.1 to 45.9	42.3	41.4 to 43.2
Severe	250	39.8	38.6 to 40.9	33.1	32.0 to 34.2
Very severe	64	40.8	38.3 to 43.2	29.8	27.4 to 32.2

Mean mental and physical health over time were plotted separately for three groups defined by their combined pain score at T0. Figure 10 shows that the groups with pain had poorer mental health score at T0 and this difference was maintained over the whole study period, although the gap between the three groups narrowed. This indicates that people with severe pain at T0 actually achieved more gain in mental health score than the other two groups, but by T3 their mean mental health score was still lower than that of the group with mild/no pain had been at T0.

Figure 10 Mean Mental Health Score Over Time by Combined Pain Score at T0

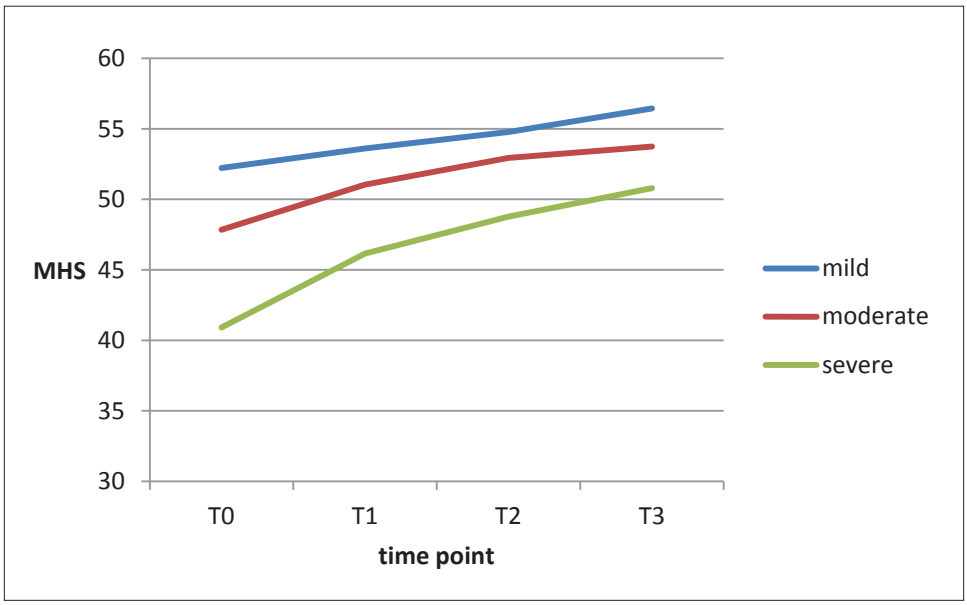
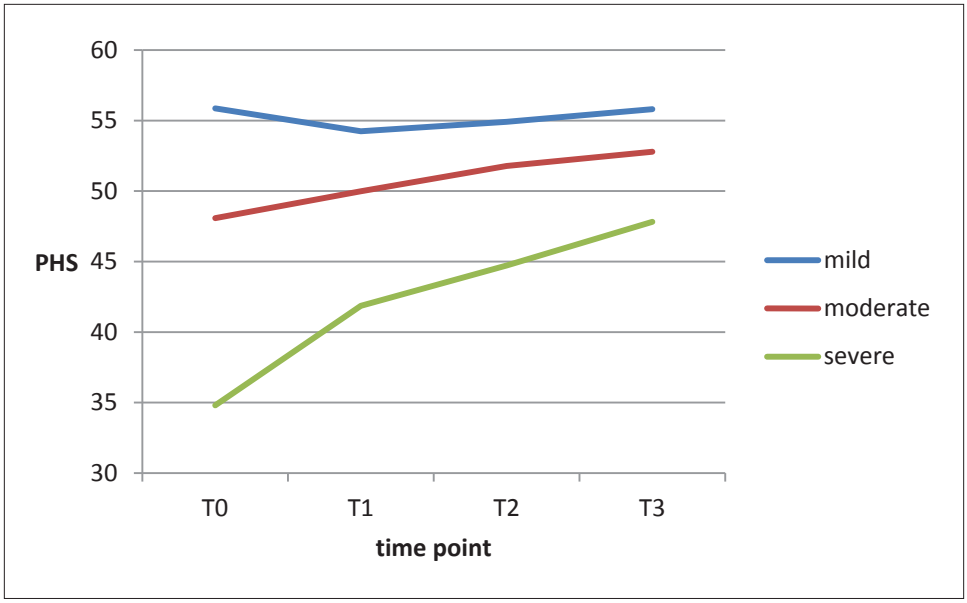


Figure 11 shows that the difference between the three groups in terms of physical health score was even more distinct. Those with severe pain had a mean score over 20 points lower than those with mild pain. In the first month, the severe pain group rapidly improved, the moderate pain improved slightly (and steadily over time) and the group with mild pain reported on average worse physical health than previously. From T1 onwards, all groups experienced a gain in physical

health, the severe pain group somewhat more rapidly than the other two, and by T3 the severe pain group had a mean physical health score similar to the score of the moderate pain group at T0.

Figure 11 **Mean Physical Health Score Over Time by Combined Pain Score at T0**



Finally, random-effects linear models were fitted to test whether quality of life outcomes were associated with pain as it varied over time. The two demographic variables associated with pain prevalence over time (functional status and wealth quintile) were included in the models. The first outcome was mental health score, adjusting for mental health score at T0, and the other covariate was combined pain score. Mental health and combined pain score varied by time whereas functional status and wealth quintile were constant. Pain was significantly associated with lower mental health score after adjusting for baseline mental health, functional status and wealth quintile (Table 29).

Table 29 **Random Effects Model Testing Quality of Life on Mental Health Score Over Time**

	Coefficient	95% CIs	Z	p
Mental health score at T0	0.33	0.29 to 0.36	19.47	<0.001
Combined pain score	–6.60	–7.21 to –6.00	–21.43	<0.001
Functional status	–3.06	–3.48 to –2.62	–13.89	<0.001
Wealth quintile	0.28	0.07 to 0.50	2.57	0.010
Constant	37.90			

For physical health score, the results were similar, but the coefficient for pain was bigger (–11.66), showing that pain had a closer association with physical health than with mental health. Results are shown in Table 30.

Table 30 Random Effects Model Testing Quality of Life on Physical Health Score Over Time

	Coefficient	95% CIs	Z	p
Mental health score at T0	0.24	0.22 to 0.27	18.73	<0.001
Combined pain score	−11.66	−12.24 to −11.09	−39.81	<0.001
Functional status	−5.42	−5.82 to −5.01	−26.03	<0.001
Wealth quintile	0.62	0.43 to 0.82	6.28	<0.001
Constant	41.22			

6.7 WHAT PREDICTS PERSISTENT PAIN AFTER THREE MONTHS OF CARE?

At T3, 16.5% of participants reported a severe combined pain score, indicating a score of either 4/5 on the POS pain item, severe/very severe pain on the MOS-HIV question 2, or pain interfering with normal life quite a bit/extremely on MOS-HIV question 3. Table 31 shows the results of bivariate analysis to find variables associated with persistent pain at T3, adjusting for facility.

Table 31 Bivariate Multilevel Models of Severe Combined Pain at T3

Variable		%	OR	p
Gender	Male Female	17.0 16.3	0.97	0.864
Age category	18–29 30–39 40–49 50–59 60–70	13.5 17.5 17.6 19.4 18.8	1.01	0.325
Education	None Began primary Began secondary diploma/ degree	24.4 16.0 16.0 15.0	0.95	0.677
Wealth quintile	Lowest Second Middle Fourth Highest	22.1 18.8 15.7 13.7 11.5	0.86	0.026
Functional status	0 1 2 3 or 4	8.6 21.7 67.9 88.9	4.72	< 0.001
Newly diagnosed	Yes No	11.2 18.6	0.61	0.020
Used ART	Yes No	14.7 12.5	1.31	0.184

Variable		%	OR	p
CD4 count	0–100	18.6	0.99	0.949
	101–200	11.8		
	201 –350	14.1		
	350+	17.2		

Poorer people, those with lower functional status, and people newly diagnosed were more likely to have persistent pain after three months under care. In particular, people with poor functional status were very likely to have unrelieved pain; 89% of those with the lowest functional status had pain at T3. In a multivariate model, time since diagnosis was no longer associated with odds of pain at T3. Severe unrelieved pain after three months was closely associated with functional status and had a weakly significant association with wealth quintile, as shown in Table 32. Less physically able people and poorer people were less likely to have adequate pain relief during the study. These are the same variables predicting severe pain at any time, in Table 26 above.

Table 32 Multilevel Model of Association of Covariates with Severe Pain at T3

	OR	95% CI	Z	P
Functional status	4.59	3.32–6.35	9.22	< 0.001
Wealth quintile	0.86	0.73–1.00	–1.91	0.056

Section 7 Discussion

This study revealed a high level of need for pain assessment and management at the facility and patient level. The integrated multiple data sources reveal urgent challenges to enhance pain relief among East Africans attending PEPFAR sites for HIV care.

The advantages of this study are its longitudinal nature and use of multiple outcomes that addressed not only pain but quality of life, and has been able to measure pain over time which is advantageous in the chronic model of HIV in which patients present with exacerbations rather than a steady and predictable decline. However, we also note that this is secondary analysis that has not used a tool with a single outcome of pain intensity or affect. The selection of the APCA African POS, which is intended to be used with single item analysis, makes the secondary analysis appropriate. The focus on both systemic and facility-based data on drug availability, and patient-reported data that drive forward the quality and outcome agenda (78), offer practical and patient-focused data for improved health care planning. The random stratified selection of sites enabled us to recruit patients from a wide range of large facilities, and this has revealed differences in pain prevalence and management. Guidance on the assessment and treatment of pain should reduce this inequity. We would also hypothesize that in smaller facilities the drug supply issues may be worse.

7.1 ANALGESIA SUPPLY

At the supply level, the data highlight the low availability of strong, and to a lesser degree, weak opioids. These cheap and effective drugs are essential to enable the WHO pain ladder to be implemented. Greater efforts are required to enhance the procurement, supply, necessary clinical training, prescribing, and stock control of these analgesics.

Recommendations

1. All facilities should be able to provide adequate analgesia for their volume of patients.
2. Advocacy is required to ensure adequate analgesia supply at the national level, with efficient in-country supply systems.
3. All pharmacies should establish stock levels to reduce stock outs of analgesics.

7.2 CLINICAL PRACTICE

The prevalence and intensity of pain underline the necessity for enhanced drug procurement and prescribing. The fluctuating and episodic nature of self-report pain requires ongoing pain assessment as part of routine care and support, and to ensure adequate pain relief , pain management should be provided onsite rather than referred out (except for complex and apparently refractory pain).

Pain assessment and control as part of integrated care and support is essential if optimal quality of life is to be achieved, as the qualitative data revealed the interaction between physical, emotional, social and spiritual pain. It is unlikely that optimal outcomes can be achieved if the patient is not treated holistically. However, the qualitative data also describe staff challenges in the assessment and management of the physical dimensions of pain.

Recommendations

1. All HIV clinical service providers should ensure that patients are regularly asked about pain as part of their ongoing assessment. Regular pain assessment is essential due to the episodic and chronic pains that can be experienced.
2. Assessment should include locally validated pain tools
3. Care and support facilities should identify local pain specialists (e.g. palliative care sites) who can offer consultancy and management of complex pain.
4. All clinical staff should be trained in the assessment, and treatment of pain using locally validated measures
5. Care and support services should be integrated as far as possible, to better reflect the multidimensional causes and effects of pain

7.3 AUDIT AND QUALITY IMPROVEMENT

The lack of focus on pain and symptoms in HIV care, treatment and support is a global phenomenon (4). However, the lower resource availability and more recent exposure to opioids as essential drugs compound the problem for patients with HIV in Africa. The use of simple, routine methods to measure and improve care processes can be readily applied in African settings (79).

Recommendations

1. Simple pain management audits should be initiated to support improved pain management, and to demonstrate successful initiatives to simply and cheaply control pain
2. Where facility systems currently maintain patient outcome information, pain data should be incorporated.

7.4 BUILDING EVIDENCE-BASED CARE AND SUPPORT

The prevalence, intensity and affect of pain among people with HIV have received little clinical research attention since the advent of ART reduced morbidity and mortality. However, the literature review and our data have revealed pain to be an important issue to patients, and a better understanding of pain and its control could make a simple, inexpensive difference to the lives of those under care.

Recommendations

1. Policy research is necessary to identify the blockages and successes in analgesia supply at the national and facility level

2. Clinical research is required to better understand the prevalence and intensity of pain at different stages in the HIV disease trajectory, especially in relation to treatment
3. Operational research and evaluation studies are urgently required to develop, test and disseminate models of better practice in the assessment and treatment of pain. Such studies should measure multiple endpoints as reflected in this analysis, including drug supply and patient-level outcomes.

7.5 SOURCES OF FURTHER GUIDANCE IN PAIN MANAGEMENT FOR HIV PATIENTS IN SUB-SAHARAN AFRICA (TO INCLUDE URLS)

- Hospice Africa Uganda Blue Book (80)
- Clinical guide to Palliative and Supportive HIV Care in Africa (81)
- The African Palliative Care Association (APCA) "Guide to Beating Pain" in Africa (39)
- Using opioids to manage pain: a pocket guide for health professionals in Africa (54)
- Guidelines for ensuring patient access to, and safe management of, controlled medicines (82)
- IMAI WHO guide, pain and symptom control guidance (44)
- The Palliative Care Toolkit (40)
- Guidance for use of the APCA African POS (83)
- The Palliative Outcome Scale (POS) (84)

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MEASURE Evaluation

Carolina Population Center
University of North Carolina at Chapel Hill
206 W. Franklin Street
Chapel Hill, NC 27516
www.measureevaluation.org

King's College London

Dept. of Palliative Care, Policy & Rehabilitation
Cicely Saunders Institute
School of Medicine at Guy's, King's & St Thomas Hospitals
Bessemer Road, London SE5 9RJ, UK
www.csi.kcl.ac.uk