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Is HIV Painful? An Epidemiologic Study of the Prevalence and Risk Factors for Pain in HIV-Infected Patients

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Abstract

Objectives—To evaluate the prevalence, impact and risk factors for pain among a cohort of HIV-infected adults treated with combination anti-retroviral therapy (cART) if indicated according to current guidelines.

Methods—This was a cross-sectional epidemiological observational study. All patients attending one HIV-outpatient centre in the UK in a 10-month period were eligible. Patients completed a validated questionnaire enquiring about demographics, HIV factors and symptoms of pain.

Results—Of 1050 eligible participants, 859 (82%) completed a questionnaire. The 1-month period prevalence of pain lasting > 1 day was 62.8% amongst whom 63% reported current pain. The prevalence of pain at most anatomical sites was broadly similar to that observed in population studies using the same questionnaires except that we found considerably higher rates of foot/ankle pain. The median duration of pain was 3 years (range 0–51 years) and the median pain score was 5.0 on an 11-point visual analogue score. Over 40% of people in pain had consulted their primary care physician and > 20% were taking analgesics daily. Independent risk factors for current pain were older age ($p=0.001$), time since diagnosis of HIV infection ($p=0.001$) and receipt of a protease inhibitor-based regimen ($p=0.04$).

Discussion—Pain, and notably foot/ankle pain, is common among adults living with prevalent HIV and is associated with substantial morbidity and healthcare utilisation.

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Competing Interests

There are no conflicts of interest from any of the authors.

Keywords

HIV; Pain; Impact; Combination anti-retroviral therapies (cART); Protease inhibitors

Introduction

Prior to effective combination anti-retroviral therapy (cART), the results of several studies suggested that severe, disabling pain affected 60-80% of people living with human immunodeficiency virus (HIV) [1–5]. However, since the advent of cART, the prognosis of HIV has been dramatically transformed with reductions in opportunistic infections and malignancies and life expectancy has normalised [6–7]. This transformed prognosis has resulted in a growing population of ageing individuals with prevalent HIV taking long-term cART who experience high levels of medical and psychiatric comorbidity [8]. Therefore, the emphasis of HIV management has changed to focus increasingly on symptoms, quality of life and prevention and management of comorbidities.

There is growing evidence that, despite cART, pain remains a common problem among HIV-infected patients [9–22]. Some, but not all, authors report prevalence rates very similar to those observed pre-cART [15–16,19]. Miaskowski and colleagues reported not only that pain was common but also that it was frequently ‘severe’ (59% of those reporting pain) [16] and Merlin et al showed that the pain was associated with significantly increased risk of impairment of physical function [19]. However, Cervia and colleagues reported lower pain intensity scores and more transient, rather than chronic, pain in 41 patients after treatment with cART [15]. There is controversy also about the role of immunological function and viral activity in the aetiology of pain. Pre-cART studies suggested that pain increased in prevalence and intensity with disease progression [5,23]. However, the findings of later studies suggested that effective cART attenuated the effects of disease stage or viral activity, as defined by CD4+ count or HIV viral load, on pain [15]. In some studies, risk factors for pain have included: female sex, lower socioeconomic status and educational attainment, depression and high rates of previous or recent use of illicit drugs [16,17]. There is also inconsistency in the literature as to whether pain is a side effect of some of the anti-retroviral therapies [10,13, 24–25]. Whilst a distal polyradiculopathy was closely linked with dideoxynucleosides in early cART regimens [26], these are generally avoidable with more modern treatment combinations. Therefore, our objective was to investigate the prevalence and distribution of pain among a UK cohort of HIV-infected adults treated according to best practice guidance with cART. We set out to quantify the prevalence of pain in the post-cART era, measure its impact in terms of intensity, effects on activities of daily living and healthcare utilisation and explore demographic, lifestyle and clinical risk factors for occurrence in order to elucidate possible strategies for prevention and treatment.

Methods

The sampling frame for this study included all HIV-infected adults who attended a routine outpatient appointment at a Teaching Hospital Centre for HIV Medicine in the UK January–October 2007. Patients were eligible if they were: aged ≥ 18 years and willing and able to

provide written, informed consent. Eligible subjects were only approached once. Patients were offered the questionnaire to complete in a private space and a trained member of the research team was highlighted as available if any additional information or assistance was required. Permission was also sought to interrogate the confidential clinical database within the centre to collect HIV-related data (date of diagnosis, route of transmission, severity and course of disease, viral load, CD4 count, cART). The study protocol was approved by the Brighton Local Research and Ethics Committee (Ref: 06/Q1907/50).

The questionnaire enquired about demography (age, sex, ethnicity), lifestyle (smoking, alcohol), and employment status. The questions about pain were those used in a number of surveys of the prevalence of regional [Urwin] and widespread pain [27–30]. All participants were asked ‘during the past month, have you had any aches or pains which have lasted for one day or longer?’ The principal risk factor analyses were based upon those reporting current pain in response to the questions: ‘do you have any such aches or pains today?’ Pain intensity was self-rated on an 11-point visual analogue scale (VAS) for the intensity of pain during the past month. Functional impact of pain was measured on another 11-point VAS in response to the question ‘in the past month, how much has pain interfered with your daily activities, rated on a scale of 0-10, where 0 is “no interference” and 10 is “unable to carry out activities”?’ The site-specific prevalence rates presented here were obtained from a series of similarly-structured questions which asked: ‘During the past 1 month, have you had any pain from your (neck; shoulder; elbow; wrist/hand; hip; knee; ankle/foot) lasting for at least 1 week’? The questionnaire also enquired about healthcare use in relation to pain in the past month. Psychological health and wellbeing were measured using the vitality and mental health domains of the SF-36 instrument [31]. Each domain was scored according to the SF-36 algorithm for each individual and the scores were investigated in tertiles of the distribution in relation to the pain outcomes: lowest tertile ‘best’ mental health (referent) and highest tertile ‘worst’ mental health).

Analysis was carried out with the SAS v9.1 statistical package. The age- and sex-specific prevalence of pain lasting for more than one week out of the past month at different sites (with 95% confidence intervals generated using the exact binomial distribution where the group size was small, or the Normal approximation where group sizes were larger), the frequency of healthcare use and self-completed score for interference of the pain with daily activities were explored. The primary endpoint for the analysis was the reporting of current pain. Initial descriptive analyses illustrated the prevalence of current pain in each patient subgroup; univariate comparisons of the prevalence of pain were performed using Chi-squared tests. Potential risk factors considered are described in Table 1 and include: sex; age, BMI, smoking status, alcohol consumption, ethnicity, mode of HIV infection, time since HIV diagnosis, the patient’s current CD4 count, HIV viral load, Centers for Disease Control (CDC) classification, and cART status. Continuous covariates (e.g. age) were initially categorised as shown in Table 1, but were subsequently included in analyses in their continuous form if appropriate; the CDC stages B and C were combined as ‘symptomatic’ as the prevalence of pain appeared to be similar in these two groups. Subsequently, factors that were identified as being associated with current pain in these univariate analyses ($P < 0.10$) were included in multivariable logistic regression analyses to identify factors that were independently associated with the outcome; factors were dropped from this model if non-

significant until a parsimonious model was reached. Current working status and SF-36 scores were excluded from these models as factors which were likely to be consequent from the pain rather than causes of it.

Results

In total, 1539 patients were registered with the Centre during the study period amongst whom 1050 patients attended one outpatient clinic. Of these, 859 (81.8%) consented to participate. A comparison of the distributions of sex, age, years since HIV diagnosis, CDC stage and exposure to cART, showed no significant differences between those who did and did not complete a questionnaire (data not shown).

In total, 775 men and 84 women, median age 42 years, completed the questionnaire. Most were Caucasian and had prolonged duration since HIV diagnosis (Table 1). Most were currently receiving cART (76.5%) and 68% had undetectable viral loads.

Pain

In total, 62.8% of respondents reported that they had experienced pain lasting >1 day in the past month (Table 2), of whom 63.3% reported pain on the day of the survey. Eighty percent indicated duration of pain >3 months and 23.6% that the pain was 'all over the body'. The median number of sites affected was 2 but the range was 0-20 separate anatomical sites in men and 0-25 in women. The age- and sex-specific prevalence of pain is summarised in Figure 1. Pain frequency and location was similar among men and women and increased with age in both sexes. The most commonly affected sites were: axial (neck and back), shoulder, and foot/ankle (Figure 2).

Impact of musculoskeletal pain

The median duration of pain was 3 years (range 1-51 years) (Table 2). The median pain intensity score recorded was 5.0 for men and 6.0 for women (mean scores 5.1 and 5.9 respectively). When asked to score the impact of pain on daily activities, the median score was 4.0 for men and 5.3 for women (mean scores 4.3 for men and 5.3 for women respectively). In total, 43.8% of those in pain reported that they had consulted in primary care because of their pain (41.7% of men and 59.7% of women). One hundred and ninety-four (22.6%) were taking analgesics most days; 70 (8.2%) had received injections of local corticosteroid; 110 (12.8%) had seen a rheumatologist, 102 (11.9%) had seen an orthopaedic surgeon and 76 (8.9%) had attended the Emergency Department to request treatment for the pain. Current pain was associated with not being in work ($p=0.0001$, 29.8% of those working vs. 53.5% of those not working reported current pain), and was strongly associated with psychological distress as measured by the SF-36 (mental health ($p=0.0001$) and physical functioning ($p=0.0001$)). Psychological wellbeing scores were significantly poorer among those with current pain (median (range) of 16 (6, 30) and 16 (5, 24) on the mental health and vitality scores respectively than among those without current pain (12 (5, 30) and 12 (4, 24) respectively)..

Risk factors for pain

In descriptive analyses (Table 1), current pain was more prevalent in older individuals, in those with an undetectable (< 40 copies/ml) viral load, in those with a longer time since HIV diagnosis, in those with more advanced CDC status, in those who had ever received or were currently receiving cART and in those on a PI-based (vs. a non-PI-based) cART regimen and in those receiving NRTIs (vs. those not receiving NRTIs). Table 3 (left-hand side) reports the unadjusted odds ratios and 95% confidence intervals for these associations. Associations were also seen with working status and the SF-36 mentality and physical functioning scales in univariate analyses (Table 1) although these factors were not included in subsequent multivariable analysis as they are likely to be the result, rather than the cause, of the pain.

Of the covariates considered, increasing age (adjusted odds ratio [aOR] per 5 years older 1.10 [95% confidence interval 1.02, 1.19], $p=0.02$), and longer time since diagnosis (aOR per 5 years longer 1.17 [1.03, 1.32], $p=0.02$) were independent predictors of current pain. Current use of a PI-based (1.39 [1.01, 1.91], $p=0.04$) regimen also remained significantly associated with current pain.

Finally, we considered whether the associations between current pain and sex and time since HIV diagnosis differed in men and women through the inclusion of interaction terms between sex and these covariates in the final model. Neither interaction term was significant (age: $p=0.27$; time since HIV diagnosis: $p=0.46$), suggesting that there was no evidence that these associations differed between sexes.

Discussion

This study confirms that the prevalence (in this case the one-month period prevalence) of pain is high in people living with HIV. The estimated prevalence rate of 63% is consistent with that reported in other studies in the cART era [14,16] and the findings of a systematic review of pain studies carried out before and after cART [22]. We found higher rates than the 39% reported by Cervia and colleagues in their US study of 41 subjects who completed pain scores before and after commencement of cART [15] but our study includes a larger population with a wide range of disease duration and longer-term exposure to cART. In keeping with the findings of some researchers [5,16], women in the current study reported higher rates of prevalence of pain than men, throughout the age range and at all anatomical sites. One study has however reported the opposite [18]. It is possible that the current study included a population that was more similar to those studied in the two (USA-based) studies than to the rural population studied by Mphahlele and colleagues in South Africa and the differences may possibly be explained by cultural or ethnic differences in occurrence or reporting of pain. Clearly, this will require additional research in other ethnic groups and countries.

The median rating for pain severity in the current study was 5.0 (95% CI 2.0-9.0) (moderately severe), a rating consistent with the results of most studies which have included a measure of pain severity [22]. Moderate-to-severe intensity pain is recognised to have a significant impact on ability to function and quality of life. Our results bear out this association as respondents scored the interference of their pain in the past month with their

daily activities a median of 4.0 (95% CI 0-9.0). This score is strikingly similar to that obtained by Breitbart and colleagues who surveyed ambulatory HIV patients in the pre-cART era and asked a similar question [5]. In 2012, Merlin and colleagues reported that pain in HIV patients was associated with a 10-fold greater risk of impaired physical function, even after adjusting for mood, age and substance abuse [19]. Our results further substantiate their conclusion that pain should be an important consideration in HIV primary care.

Overall, 35.5% of those with pain reported taking analgesics most days. Inadequacy of pharmacological pain management has been reported in previous studies among HIV-infected patients. Using pain management indexes (PMI), other investigators have reported sub-optimal effectiveness of pain management in the majority (66-100%) of respondents [22]. Although we did not include a PMI in this study, we were able to explore the percentage of people reporting pain receiving no treatment for pain, a measure used by other researchers as a marker of inadequate pain management. We found that 64.5% of our respondents in pain were not taking analgesics most days, a rate similar to that observed by others (40-73%) [22]. However, further exploration revealed that those taking analgesics most days rated their pain as more intense on a VAS and rated the interference of their pain with their daily activities as greater than those not taking analgesics most days. Our study design does not allow us to investigate whether patients have been prescribed analgesics and are choosing not to take them regularly perhaps because of toxicity or inefficacy, or because they believe their symptoms are insufficiently severe. Therefore, future research could usefully explore prescription and adherence with prescription of analgesia and the reasons for which patients do/do not take the medications regularly if we are to better understand how to manage pain in HIV.

In accord with the results of other studies [17,19,21], we found that pain in HIV was strongly associated with psychological ill-health ($p<0.0001$). Merlin and colleagues have demonstrated this in several studies and have also shown that there is a strong interaction between pain, mood, substance abuse and lower socioeconomic status [17,19,21]. They also showed that people in pain were more likely to miss clinical appointments but only if they were not substance abusers [17]. Failure to attend appointments has important implications for medication adherence and treatment success in HIV. Our survey did not allow characterisation of socioeconomic status in great detail but we found a much higher proportion of worklessness amongst those reporting pain than among those without pain ($p<0.0001$) and recognise the significance of worklessness as a factor importantly associated with poverty and socioeconomic status.

One of our aims was to explore the impact of parameters of HIV infection on pain. We found that duration of diagnosis of HIV was associated with pain and, in univariate analyses only, symptomatic stage of infection and cART exposure were also associated. Other studies have explored these parameters and produced inconclusive findings: for example, whilst the results of three studies suggested higher prevalence of pain with more advanced stage of infection [32–34], three others found no such association [5,35–36]. Moreover, two studies [14,37] found a higher prevalence of pain amongst those with lower CD4+ counts and one showed more pain sites among those with lower CD4+ counts [32], three others failed to see associations with CD4+ counts [5,35,38]. We found no association with viral loads or CD4+

counts in this study but recognise that we were only able to explore the effects of the most recent results and that associations may have been present with nadir counts, which were not available for these participants. Some, but not all, studies have implicated cART in pain. Breitbart et al who studied patients commencing cART, reported beneficial effects of cART on pain [5], whilst Richardson and colleagues reported no difference in rates of pain [37]. In the current study, PI use was associated with pain ($p=0.04$) in univariate, but not multivariable models. In clinical trials of PIs amongst naïve HIV-infected patients and non-infected patients as post-exposure prophylaxis, symptoms of muscle pain and joint pain are relatively commonly (10-30% incidence) reported but usually described as 'mild' and 'self-limiting' [24,39]. Of interest, PIs have been implicated as a cause of pain in another study of female HIV patients [37]. Given that we had relatively numbers of female participants, this study was not powered to investigate a gender effect further and more research will be needed. Notably, use of PIs was recently shown to be associated with increased risk of peripheral neuropathy [40]. It is possible that PIs have some effect on peripheral or central pain pathways but more research into the long term impact of PIs will be required.

This study included specific questions about pain at different anatomical sites, which allowed comparison of pain at different regional sites with those obtained from UK and US general population surveys [27,41]. Broadly, the rates of prevalence and distribution were similar among those with HIV to those found in the general population with the exception of the results at the foot/ankle where we found much higher rates of pain prevalence. We hypothesise that this may reflect the common occurrence of peripheral neuropathy amongst HIV-infected adults. Some of the burden of neuropathy was caused by the neurotoxicity of some nucleoside analogue reverse transcriptase inhibitors (NRTI), particularly stavudine, didanosine and zalcitabine however other HIV factors have been implicated including older age, co-infection, co-existent diabetes mellitus and TB therapy with isoniazid. A recent study found that 32.1% of 2141 subjects starting cART had evidence of a peripheral neuropathy after 3 years of follow-up [40] despite excellent levels of viral and immunological control. It has been shown that the majority of patients (50-90%) with HIV-associated sensory neuropathy experience pain, proportions that are greater than in other common types of peripheral neuropathy such as diabetes and that recognition and treatment of painful sensory neuropathy in HIV is frequently sub-optimal [42]. Interestingly, people with more advanced HIV infection have been shown more likely to report pain with their neuropathy [43–44]. This epidemiologic study does not allow investigation of the aetiology of pain but we hypothesise that much of the excess reporting of foot/ankle pain in this study might be related to underlying sensory neuropathy.

The findings of this study must be taken alongside several limitations. This was a cross-sectional study so that the associations reported were cross-sectional and do not allow speculation about cause or effect or direction of association. Whilst the response rates were excellent (82%), and comparison of some of the key characteristics between those who did/did not complete the questionnaire revealed no significant differences, we cannot rule out the possibility that those who chose to complete the questionnaire were those who considered themselves affected by musculoskeletal symptoms and that the estimated prevalence rates reported are therefore relative over-estimates. These results were found from our survey among a well-characterised cohort of HIV-infected adults attending one UK

centre for their HIV care. However, this cohort of patients may differ from those attending other HIV centres in the UK and elsewhere. For example, most of this cohort are male and Caucasian and most acquired HIV through sexual contact. We cannot exclude the possibility that there are factors peculiar to this cohort that also affect musculoskeletal pain that are not generalisable to patients infected with the virus through different modes of transmission or from different ethnicities. For example, we showed no statistically significant association between mode of transmission of HIV and pain in the current study but other investigators found that mode of transmission was important and, in particular, that intravenous drug use was associated with higher pain levels and pain at a higher mean number of sites [32,35]. Our cohort only included 8 subjects known to have been infected by intravenous drug use so that this study was under-powered to detect this association. Similar studies will need to be carried out in different HIV cohorts to see if our findings are generalisable.

Our results suggest that duration of HIV diagnosis is importantly associated with pain and this may reflect a number of factors: immunological function and viral activity; increasing burden of physical and psychological co-morbidities; increasing numbers of non-HIV medications; reduced resilience to side effects. Current immunological function and viral activity were investigated using the most recent CD4+ cell count and viral load for each subject and showed no important relationships with pain. However, it may well be that disease status might be more usefully represented by nadir CD4+ count, as a marker of disease state at its worst, rather than recent count and it is a limitation of this study that these data were not available for this cohort of patients. Further research will be needed to clarify the role of disease stage and viral activity on pain in cART treated patients. This study was also not designed to collect information about non-HIV morbidities or medications used for other diseases so we are also unable to investigate the role of those factors.

In summary, we have reported the results of a large-scale epidemiological survey of the occurrence of musculoskeletal pain in HIV-infected adults and found that it is a very common symptom associated with substantial morbidity and that feet/ankles are more commonly affected than in other populations. Cross-sectionally, the risk factors were age and time since diagnosis of HIV. Current use of protease inhibitors may be associated with pain but further research is warranted.

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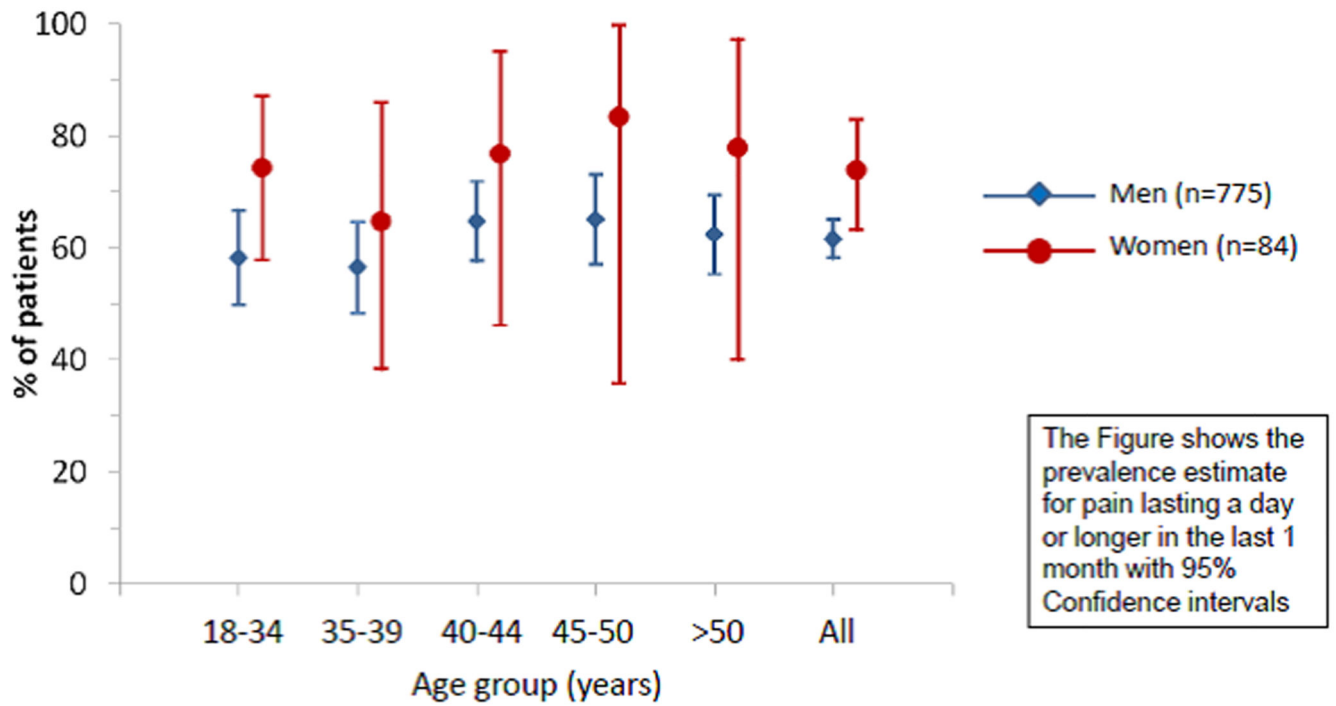


Figure 1. The cross-sectional age- and sex-specific prevalence of musculoskeletal pain among 859 adults infected with HIV

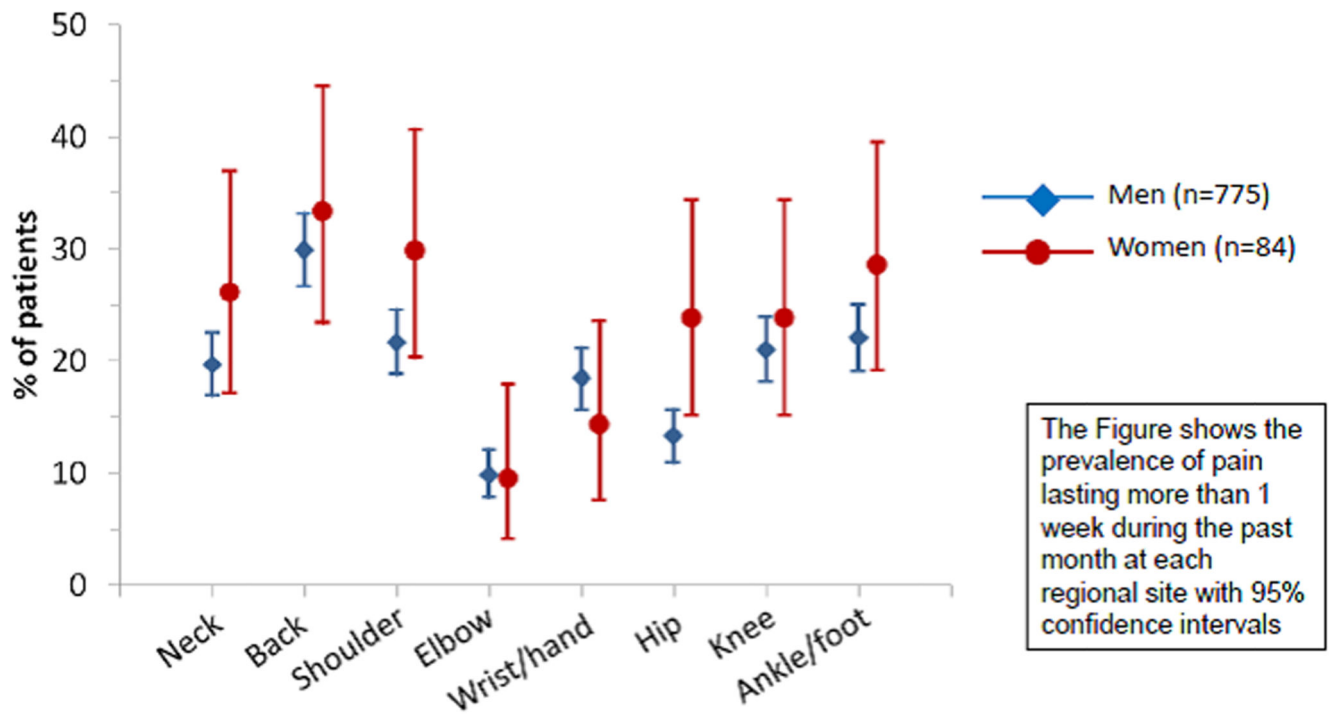


Figure 2. The cross-sectional site-specific prevalence of musculoskeletal pain among 859 adults infected with HIV

Table 1
(i) Demographic and (ii) clinical characteristics of HIV-infected study participants, and the proportion of each group currently experiencing pain (n=859 unless otherwise stated)

(i) Demographic characteristics		Number (% of total sample)	Number with current pain (%)	p-value [†]
n		859 (100.0)	341 (39.7)	
Sex	Male	775 (90.2)	303 (39.1)	0.33
	Female	84 (9.8)	38 (45.2)	
Age (years)	Median (range)	42 (19 - 77)		0.002
	19-34	171 (19.9)	49 (28.7)	
	35-39	164 (19.1)	56 (34.2)	
	40-44	186 (21.7)	80 (43.0)	
	45-49	143 (16.7)	65 (45.5)	
	50	195 (22.7)	91 (46.7)	
Ethnicity (n=833)	White	631 (75.8)	261 (41.4)	0.35
	Black African	84 (10.1)	27 (32.1)	
	Other	118 (14.2)	43 (36.4)	
BMI (kg/m ²) (n=810)	Underweight (<18.5)	40 (4.9)	17 (42.5)	0.99
	Normal (18.5, <25)	497 (61.4)	197 (39.6)	
	Overweight (25, <30)	204 (25.2)	81 (39.7)	
	Obese/morbidly obese (30)	69 (8.5)	26 (37.7)	
Smoking status (n=850)	Current	348 (40.9)	138 (39.7)	0.71
	Ex-smoker	266 (31.3)	112 (42.1)	
	Never smoked	236 (27.8)	88 (37.3)	
Consume alcohol	No	198 (23.0)	88 (44.4)	0.14
	Yes	661 (77.0)	253 (38.3)	
Hepatitis B +ve	No	843 (98.1)	334 (39.6)	0.94
	Yes	16 (1.9)	7 (43.8)	
Hepatitis C +ve	No	848 (98.7)	336 (39.6)	0.93
	Yes	11 (1.3)	5 (45.5)	
Working status (n=852)	Working	486 (57.0)	145 (29.8)	0.0001
	Not working	366 (43.0)	195 (53.5)	
SF-36 Mentality	Median (IQR)	14 (5, 30)		0.0001
	5-11	264 (34.1)	68 (25.8)	
	12-16	254 (32.8)	97 (38.2)	
	17-30	256 (33.1)	144 (56.3)	
	Physical functioning	Median (IQR)	14 (4, 24)	
	4-11	266 (34.6)	59 (22.2)	0.0001
	12-16	281 (36.5)	121 (43.1)	
	17-24	222 (28.9)	126 (56.8)	

(ii) Clinical characteristics

		Number (% of total sample)	Number with current pain (%)	p-value ¹
n		859	341 (39.7)	
Mode of infection	MSM ²	217 (25.3)	84 (38.7)	0.66
	Other	60 (7.0)	21 (35.0)	
	Not known	582 (67.8)	236 (40.6)	
Latest CD4 (cells/mm ³) (n=837)	Median (range)	475 (12, 1407)		0.99
	<200	59 (7.1)	24 (40.7)	
	200-349	164 (19.6)	66 (40.2)	
Latest viral load (copies/ml) (n=842)	Median (range)	40 (40, 834687)		0.02
	40	569 (67.6)	242(42.5)	
	>40	273 (32.4)	93 (34.1)	
Time since HIV diagnosis (years) (n=839)	1	88 (10.5)	24 (27.3)	0.0009
	>1, 3	132 (15.7)	38 (28.8)	
	>3, 5	133 (15.9)	51 (38.4)	
	>5, 10	216 (25.7)	98 (45.4)	
	>10, 20	220 (26.2)	99 (45.0)	
CDC status (n=839)	A – asymptomatic	489 (58.3)	171 (35.0)	0.01
	B – symptomatic	190 (22.7)	89 (46.8)	
	C – AIDS	160 (19.1)	71 (44.4)	
cART naive	Never had cART	154 (17.9)	46 (29.9)	0.008
	Have had cART	705 (82.1)	295 (41.8)	
Current ART status	Not on cART	202 (23.5)	66 (32.7)	0.02
	On cART	657 (76.5)	275 (41.9)	
	PI based – No	580 (67.5)	209 (36.0)	0.002
	PI-based - Yes	279 (32.5)	132 (47.3)	
	NNRTI based - No	503 (58.6)	201 (40.0)	
	NNRTI based –Yes	356 (41.4)	140 (39.3)	
NRTI-based – No	259 (30.1)	90 (34.8)	0.91	
NRTI-based - Yes	600 (69.9)	251 (41.8)		

¹ p-value obtained from a univariate comparison of the proportions currently experiencing pain in each group (Chi-squared test).

² MSM: men having sex with men; CDC: Centers for Disease Control; cART: combination antiretroviral therapy; ART: antiretroviral therapy; PI: protease inhibitor; NNRTI: non-nucleoside reverse transcriptase inhibitor; NRTI: nucleoside reverse transcriptase inhibitor

Table 2
Musculoskeletal pain and its impact among 859 HIV-infected adults

	Total (n=859)	% of total
Ever had pain lasting at least 1 day in the last month	539	62.8
Number of painful sites (range)	6 (1-25)	-
Seen a Rheumatologist for pain	110	12.8
Seen an orthopaedic surgeon for pain	102	11.9
Attended Emergency Department for pain	76	8.9
Use analgesics most days for pain	194	22.6
Had an operation because of pain	40	4.7
Of those in pain:		
Currently in pain	341	39.7 (63.3 of those with pain)
Pain lasting >3 months (chronic pain)	431	50.2 (80.0 of those with pain)
Time off work due to pain	44	5.1 (16.2 of those with pain)
Seen a doctor because of the pain	236	27.5 (43.8 of those with pain)
Median duration of pain (years)(range)	3 (1-51)	-
Median pain score (range)	5 (1-10)	-
Mean pain score (SD)	5.2 (2.2)	-
Median disability score (range)	4 (0-10)	-
Mean disability score (SD)	4.4 (2.9)	-

Table 3
Associations between demographic and clinical factors and current pain from univariate and multivariable logistic regression analyses

Characteristic		Unadjusted OR (95% CI)*	p-value	Adjusted OR (95% CI)	p-value
Age	/5 years older	1.12 (1.05, 1.20)	0.0008	1.10 (1.02, 1.19)	0.02
Time since HIV diagnosis	/5 years	1.26 (1.13, 1.41)	0.0001	1.17 (1.03, 1.32)	0.02
Viral load (copies/ml)	>40	1			
	40	1.43 (1.06-1.93)	0.02	-	
HIV stage	Asymptomatic (CDC stage A)	1			
	Symptomatic (CDC stages B/C)	1.57 (1.18, 2.07)	0.002	-	
cART naive	No	1			
	Yes	0.59 (0.41, 0.86)	0.006	-	
Currently on cART	No	1			
	Yes	1.48 (1.06, 2.07)	0.02	-	
On NRTI	No	1			
	Yes	1.35 (1.00, 1.83)	0.05	-	
On PI	No	1		1	
	Yes	1.59 (1.19, 2.13)	0.002	1.39 (1.01, 1.91)	0.04

* OR: odds ratio; CI: confidence interval; CDC: Centers for Disease Control; cART: combination antiretroviral therapy; NRTI: nucleoside reverse transcriptase inhibitor; PI: protease inhibitor.