Self-management interventions for pain and physical symptoms among people living with HIV: a systematic review of the evidence

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Conflict of Interest

AW reports personal fees from Advisory boards or speaker fees from GSK, ViiV Healthcare, Gilead Sciences and Janssen, grants from Grants to Imperial College London from Gilead Sciences, ViiV Healthcare, Janssen, BMS and Merck, outside the submitted work.

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Introduction

Evidence shows a substantial decline in mortality among people living with HIV (PLWH) resulting in increased life expectancy [1, 2]. PLWH experience a high burden of pain and physical symptoms. It is hypothesised that PLWH experience pain due to severity of their underlying HIV infection and side effects of HIV treatment [3]. Recent evidence also suggests inflammation as a potential aetiology [4]. A systematic review of pain in HIV/AIDS reported that pain prevalence ranges from 54% (point prevalence) to 83% (three-month period prevalence) [5]. Peripheral neuropathy (PN) is common in HIV infection despite the use of effective ART [6], with a prevalence range of 44%-60% [7-9]. Longitudinal studies conducted in high income countries report that the prevalence of PN is increasing despite the decline in use of neurotoxic drugs [10, 11]. An observational cohort study reported a prevalence of mild PN of 38%. It is often under recognised and, given the increased survival of PLWH, the prevalence of this problem is actually greater than the historically-reported rates of severe PN from studies conducted prior to ART [12]. Pain is considered chronic if it has a duration of at least three months beyond the period of normal healing [13]. Pain in HIV is often undertreated, underreported, and unlikely to be routinely assessed [14].

PLWH also experience a high burden of physical symptoms [15, 16] from diagnosis [17, 18], in advanced disease and while on active ART [15, 19]. Common symptoms include fatigue (61%-72%) [8, 20, 21], headache (31.8%-42%) [7, 22, 23], anorexia (44%-49%), nausea/vomiting (25%-50%), diarrhoea (6%-54%), and weight loss (8%-89%) [8, 17, 18, 22, 24], pruritus/itching (67%) [8, 17], chills, rash (32.8%-50.4%) [22, 23, 25], sweat, fever (32%-89%) [18, 21], dyspnoea (30.8%) [18, 21-23], and cough (53%) [8, 18, 22].

Pain and physical symptoms are associated with poor drug adherence [26, 27], viral load rebound, [19], poor quality of life [28-31], and distress [32-34]. Furthermore, patients in pain are likely to be involved in risky behaviours such as alcohol use, intravenous drug use [5, 22, 35], and sexual risk taking [36]. Pain experience also results in treatment switching

[37, 38], and suicidal ideation [18, 39].

Self-management intervention include activities individuals take for themselves and their families to stay fit and maintain good health [40]. Evidence-based self-management interventions have the potential to help PLWH to successfully monitor pain and physical symptoms [41].

Although there is some evidence from a systematic review that self-management interventions have positive effects in improving physical, psychosocial, knowledge and behavioural outcomes among PLWH [42], this review covered studies conducted until 2010, focused on educational interventions only and excluded studies conducted in Africa. This removes the opportunity for us to learn from effective interventions that may have potential for replication in high income/developed countries (south to north learning). Furthermore, little is known about the effective methods of supporting caregivers in their role in pain and symptom management among PLWH.

We aimed to systematically identify and appraise the evidence regarding the effectiveness of self-management interventions for pain and/or physical symptoms for PLWH and/or their caregivers.

Methods

Search strategy and selection of studies

The full protocol is registered with PROSPERO, number CRD42017055857 [43]. We searched in Amed, Assian, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Library, Embase, Medline, PsycInfo, Scopus and Web of Science from 1984 (when HIV was first reported) to May, 2018. Key words and subject headings were used (see table 1). Key words/concepts for pain and physical symptoms were based on the Revised Sign and Symptom Check-List for HIV [29], which captures physical symptoms including those related to the impact of HIV treatment [29]. Reference lists of identified papers were hand searched.

Subject headings and word truncations were entered according to requirements of each database to map all possible keywords. HIV was combined with AIDS using the 'OR' function (Group 1). All the interventions were combined using the 'OR' function (Group 2). Pain and symptoms were combined using the 'OR' function (Group 3). Finally search strategies 1, 2 and 3 were intersected using the 'AND' function.

We included studies which recruited PLWH and informal caregivers, any self-management interventions, published randomised/non-randomised trials written in English language, and studies reporting pain and physical symptom outcomes. We excluded studies that recruited patients without HIV diagnosis, and formal caregivers, unpublished studies, and qualitative studies, studies without a comparison group (see table 2).

A PRISMA flow chart (see figure 1) reports the study selection process [44]. All references from the initial database and hand searching were exported to Endnote version 6, and the database was de-duplicated. KN independently evaluated all references by reviewing titles and abstracts according to the inclusion and exclusion criteria. If the title and abstract were clearly irrelevant the reference was excluded. The full text of retained references was obtained and the content reviewed against the inclusion and exclusion criteria. Any reference for which inclusion and exclusion criteria were unclear was discussed with a second reviewer (RH). Disagreements between the reviewers were resolved through discussion with the review team.

Data extraction

KN extracted data from studies using methods described in the Cochrane handbook for systematic reviews of interventional studies [45]. A standardised data extraction form was used to ensure consistency in the review [46]. The review team checked data extraction based on the standardised form and any queries were resolved through discussion.

Methodological quality of the studies

KN assessed the quality of each study independently using the Joanna Briggs Institute Critical Appraisal checklist for Randomised and non-Randomised trials (see table 7) [47]. RH checked the critical appraisal, and discrepancies in the assessment for quality were resolved through discussion. Table 3 provides summary of quality assessment of each study. GRADE was used to rate the quality of each outcome (table 4) [48].

Many studies did not provide sufficient details to allow a detailed assessment of methodological quality. Nine studies were judged "adequate" on randomisation procedures [49-58], while seven studies did not report methods of randomisation [59-65].

Three studies blinded participants by use of a dummy intervention [50, 51, 59]. In the first study, participants in the intervention wore earphones and listened to tapes with instructions to elicit a relaxation response, while participants in the control group wore earphones and listened to soft music routinely played in the clinic [50]. In the second study, participants in the intervention group attended six educational sessions on diarrhoea management using food, while the control group also attended educational sessions on general self-care and healthy living with HIV [51]. In the third, participants in the intervention arm received a symptom management manual while participants in the control arm received a general nutritional management manual. Both manuals were similar in size [59].

Five studies reported blinding of outcome assessors [52, 56, 58, 63, 64]. Allocation concealment of the person randomising participants was reported in six studies [50, 51, 54-57, 66]. Collection of outcome data differed in these studies; five studies collected data via self-administered questionnaires [49, 59, 60, 64, 67], two studies used online data collection [54, 57, 67], and two studies used postal questionnaires [60, 64]. Seven studies reported attrition rates ranging from 24%-34.6% [50, 51, 54, 57, 59, 66-68].

Intention to treat analysis (ITTA) was only applied in four studies [50, 58, 59, 65]. The remaining studies excluded all participants lost to follow-up. However two studies [49, 55]

did not provide details about losses to follow-up, including methods of handling this in analysis.

Quality of evidence

Quality of evidence was moderate for pain severity, pain interference, and symptoms of diarrhoea and low for physical symptoms, quality of life, and knowledge outcomes. Evidence was very low for symptoms of fatigue and weight loss/gain. All these outcomes are patient reported and were downgraded due to serious risk of bias from lack of blinding and insufficient details about randomisation methods, and attrition. Quality of evidence was further downgraded because of serious inconsistency due to heterogeneity of the participants, interventions and use of tools without established psychometric properties.

Findings

Characteristics of the studies

A total of 22 papers, reporting 19 different studies, met the inclusion criteria (three studies were reported in two papers each). Tables 5 and 6 presents detailed data on each study. The total number of participants was n=2189 patients and n= 218 caregivers. The majority of studies were conducted in high-income countries (n=15), predominantly in the USA.

Of the 19 studies, 17 were RCTs and two used quasi-experimental designs [67, 68]. Sample size ranged from 27 [58] to 775 [59]. Two RCTs recruited both patients and family caregivers [56, 64]. Most studies allocated participants to one of the two arms, but three studies randomised to three arms [49, 61, 64, 69].

The interventions included face-to-face sessions (15-90 minutes) combined with information leaflet/booklet and work book for participants to take away with them [55, 56, 58, 59, 63, 65]. Two studies delivered an intervention online [54, 57, 67]. Three studies used cell phones or phone call to provide the intervention exclusively [53] or as a reinforcement [56, 69].

Nine studies were delivered by health care professionals [51, 52, 56, 67], while four were delivered by peer-leaders [54, 58, 60, 65]. None of the studies reported data on cost effectiveness of the interventions. Duration of follow-up varied from three weeks [51] to 24 weeks [51].

Pain and physical symptom outcomes

Three studies reported data on pain severity as a primary outcome, and two studies reported data on pain interference as a secondary outcome. Only one study found significant differences on pain severity and interference [56]. Nkhoma et al (2015) used the Brief Pain Inventory and found significant differences on pain severity and pain interference between a nurse-led pain educational intervention (consisting of an information leaflet, face-to-face discussion and a phone call) and usual care [56]. Nkhoma et al (2015) trial was a one-off intervention and participants were follow-up at eight weeks. Parker et al (2016) used the BPI-Xhosa and found no significant differences between a peer-led exercise and education intervention and usual care on pain severity and interference [58]. Parker et al (2016) trial consisted of two-hourly sessions and workbook on self-management of pain and physical symptoms for six weeks. Questionnaires were administered monthly for four months. Gifford et al (1998) assessed pain with the Medical Outcomes Study and found no significant difference between a peer-led positive self-management programme (PSMP) intervention and usual care [60]. The intervention consisted of seven interactive health education group sessions on self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition. Participants were followed-up at three months. The quality of evidence from studies which assessed pain outcomes was moderate, the quality was downgraded due to risk of bias following lack of blinding.

Symptom severity and frequency was reported in eight studies [53, 54, 59, 60, 62, 64, 65, 67] Three of the eight studies reported significant decrease in symptom severity [53, 59, 60] and frequency [53, 59]. Vidrine et al (2007) used the HIV related symptom status

and reported a significant decline in symptom frequency and burden among the intervention group compared to the control group [53].

Wantland et al (2008) used a revised sign and symptom checklist to evaluate symptom frequency and intensity and reported a significant decrease in symptom frequency and intensity among the symptom management manual group compared to the nutritional management manual group [59]. In a positive self-management programme (PSMP), Gifford et al (1998) created their own instrument to assess symptom severity and reported significant improvement in the intervention group compared to the control group [60].

However Webel (2010) who randomised HIV positive women to receive a positive self-management programme (PSMP) developed by Gifford et al (1998) or HIV symptom management manual developed by Wantland et al (2008) failed to demonstrate effectiveness of the intervention [65]. Likewise Inouye et al (2000) reported non-significant results between the self-management training and education programme intervention and usual care [62]. A positive outlook peer-led online-self management intervention among gay men reported nonsignificant results on physical health and symptoms [54, 57]. Pakenham et al (2002) used the brief symptom inventory and reported a non-significant decrease in symptom distress between two intervention groups and the control group [64]. A non-randomised online self-management intervention study assessed symptoms with the HIV symptom index, but did not observe significant differences between the self-management skills sessions and traditional care [67].

Symptoms of fatigue were examined in two studies [49, 60], with one study reporting that the guided imagery intervention showed a significant decrease in fatigue compared to the relaxation response intervention and usual care [49].

Symptoms of weight loss and gain were examined in two studies which evaluated effect of self-management dietary interventions on weight [55, 68]. One study was interested in weight loss [55], while another was interested in weight gain [68]. Both studies showed significant effects of a diet programme on weight.

Symptoms of diarrhoea were reported in one study. This was a nurse-led dietary intervention. Participants were instructed to eat a low fat, lactose free, low insoluble fiber, high soluble fiber, and caffeine-free diet, including preparation of tasty foods in line with the diet, strategies to keep the diet cost-efficient. Comparison group were provided with standard information on safe-care and healthy living with HIV-AIDS, without information about diet, and received the intervention after completion of the study. Both groups attended six study sessions, with measurers administered at three and 24 weeks. The intervention group reported significant improvement in stool frequency and consistency at three weeks and 24 weeks [51].

Symptoms of oral candidiasis were reported in one study. A dentist delivered intervention reported that oral hygiene and instructions showed non-significant effects on recurrence of oral candidiasis, self-diagnosis, prevalence of candidiasis [63].

Sleep duration and quality was reported in one study [52]. A nurse and health educator delivered the intervention on management of HIV and sleep related problems. The study reported non-significant effects on sleep duration, sleep efficiency, sleep fragmentation, disturbances and sleep impairments.

Quality of life and knowledge outcomes

Quality of life was reported in nine studies [52, 54, 56, 57, 62, 64-66, 69]. Four studies reported statistically significant effects of the intervention on some subscales of quality of life [56, 57, 64, 69]. Knowledge outcomes were reported in six studies [54, 56, 57, 60, 61, 64], with four studies reporting statistically significant effects [56, 57, 61, 64] while two reported no effects [54, 60].

Outcomes for caregiver participants

Two studies randomised both patients and caregivers. One was conducted in Malawi [56] and another one in Australia [64]. The Malawian study was a two arm trial (details provided on pain severity and interference outcomes), while the Australian study was a three arm trial. In the Australian study, caregivers in arm 1 received the intervention

with their patients, caregivers in arm 2 received the intervention, but not their patients, and caregivers in arm 3 received standard care. The intervention consisted of eight weekly sessions of one and half hours conducted by psychologists. Based on two HIV target problems which participants stated.

Both studies reported significant improvement in knowledge and quality of life outcomes [56, 64]. Furthermore, Nkhoma et al (2015) reported significant improvement in caregiver motivation to provide care. Pakenham et al [50] reported data on caregiver global distress. Caregivers who received the intervention with their patients (arm1), experienced significant improvements in global distress compared to caregivers who received the intervention alone (arm2) and caregivers who received standard care (arm3). However, social adjustment did not differ significantly between the three groups.

Discussion

Despite the clinical burden of pain and physical symptoms among PLWH, this systematic review identified only three studies that examined the effects of self-management interventions on pain outcomes and eight studies on physical symptom outcomes. Most of the studies reviewed were of low quality due to risk of bias and inadequate reporting [49, 53, 55, 59, 62, 65, 67, 68, 70]. Most of the included studies were conducted ten years ago [49, 51, 53, 59, 61-66, 68-70] and predominantly in the USA [49, 51, 53, 59, 62, 63, 65, 70].

Two studies with positive outcomes delivered the intervention once [59], however in most of the studies [49, 53, 55, 61, 64, 66, 69] participants had multiple exposure to the intervention. We therefore can say that both one off intervention and ongoing sessions were effective. Studies with positive results had short-term follow-up (six and 12 weeks) [53, 55, 57, 59, 61, 64, 66, 69]. Some studies conducted a one off follow-up assessment [49, 53, 55, 61, 69]. It is therefore difficult to infer if the positive benefits observed could

be sustained over time. Some studies conducted multiple follow-ups [51, 57, 59, 66]. In Wantland et al,(2008) study, symptom prevalence significantly declined at week four with a further significant decline at week 12 [59] . Likewise, Anastasi et al, (2006) study, the intervention showed significant improvement at week three and this was further significant at week 24 [51]. However, in Millard et al; 2016 study, some quality of life sub-scales (emotional distress) were significant at week eight, but not significant at week 12. Body change and social relationships were not significant at week eight, but were significant at week 12. In the same study, the intervention showed significant improvements in constructive attitudes and approaches, skill and technique acquisition, and health service navigation at week eight, but these were not significant at week 12 week. Furthermore, the intervention group improved significantly on self-management skills, Positive outlook self-efficacy (POSE): at week 8, relationships, social participation and emotions, but these were not significant at week 12.

We therefore can say that in some studies positive outcomes were sustained over time, while in some studies they were not sustained. Furthermore, in some studies it is difficult to know because they conducted one-off follow-up assessment.

Among caregiver participants, only two studies reported data on caregiver outcomes with both studies reporting statistically significant results across most outcomes. There is some evidence to suggest that self-management interventions delivered either online/computer-based, face-to-face discussion or group-based including booklet, leaflet or manuals are effective in improving pain and physical symptoms. These results are in line with findings from systematic review of person-centred pain management educational interventions in cancer population [71, 72].

Based on these findings, there is limited evidence that self-management interventions among HIV-infected individuals with chronic pain and high burden of physical symptoms are effective.

Interestingly studies which used cheap and locally available resources (such as food locally available to self-manage diarrhoea, or information leaflets) [51, 55, 68] were effective compared to some technology based interventions such as computer sessions [54, 67]. Although some self-management interventions were not effective, but they helped to promote health behaviours such as modification of food habits by reducing sugar meals thereby preventing dental caries [63], likewise physical exercises meant to reduce symptoms but do help in reducing weight and preventing cardiovascular conditions [60].

There is a very well established self-management literature of chronic diseases such as diabetes [73], as well as self-management of pain, physical and emotional functions, and quality of life among patients with chronic back and musculoskeletal pain and various disease conditions [74-78]. Self-management is useful in other populations and for other outcomes, but there is little high quality research on the topic in HIV population. Self-management of pain and symptoms in PLWH is still a new field with lots of work to be done.

Behavioural change was the main focus of the theoretical approaches used in the studies reviewed. Banduras self-efficacy theory [79] was frequently used with an underlying premise that patients' belief in their own ability to accomplish a specific health behaviour or achieve a reduction in pain or symptom severity and frequency leads to improved health outcomes [80, 81].

This review provides a better understanding of the state of science and potential areas for future research on the effectiveness of self-management interventions for PLWH and their caregivers. Future research areas include self-management interventions using theoretically plausible models for adults with HIV/AIDS and self-management interventions for adolescents with HIV/AIDS. There is a need to conduct well-designed multi-centre and national trials to evaluate their effectiveness since evidence from these studies reviewed mostly focused on one region with few study sites.

This is the first review of self-management interventions in HIV population to include studies conducted across the globe, focussing on different models of self-management and targeting patients and their informal caregivers.

Studies reviewed were not adequately explicit about methods in order to judge the quality of evidence. Sample size was very small in most of the studies reviewed and a high attrition rate was also common in these studies. There was a great degree of heterogeneity in the studies therefore it was inappropriate to pool data due to differences in nature and context of the interventions, instruments used, duration of the interventions and period of follow-up.

The review has identified interventions with potential and gaps in evaluation methods for self-management interventions in HIV/AIDS population.

Conclusions

Given the high prevalence and burden of pain and physical symptoms among PLWH, and the clinical and public health implications of this, relatively few studies and fewer recent ones [52, 54, 56-58, 67] were identified in this review. Only three studies assessed pain as an outcome, and one of these reported significant results. The included studies differed largely in several aspects including clinical settings, outcome measures and assessors, type of the intervention, duration of the study and type of symptoms.

There is some evidence to suggest that self-management interventions delivered either online, face-to-face or group-based consisting of booklet, leaflet or manuals are effective in improving pain and physical symptoms. However caution is needed when interpreting these studies because the quality of evidence is relatively poor due to methodological weaknesses of some designs related to small sample sizes [58, 62-64, 70], high attrition rate [50, 51, 54, 59, 66-68], and use of instruments without established psychometric properties [54, 57, 60]. We recommend modelling a theoretically plausible, feasible and

acceptable intervention for pain and symptom self-management among culturally diverse people with HIV using an RCT design.

Authors contributions

All authors contributed to and approved the systematic review protocol. KN conducted the search. KN and RH extracted data, assessed risk of bias and graded the evidence. CN verified data extraction where necessary. All authors then reviewed data extraction and contributed to interpretation. KN drafted the manuscript. All authors reviewed the manuscript and each made a significant contribution to successive drafts. All authors approved the manuscript.

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Table 1: search strategy

Search strategy stage number	Key concepts	Key words
1	HIV AIDS	HIV or human immune deficiency virus, human immunodeficiency virus AIDS or Acquired immune deficiency syndrome or Acquired Immunodeficiency syndrome
2	Interventions	Self-management or self-help or self-care or patient education or patient teach* or patient inform* or patient train* or caregiver$ education or caregiver$ teach* or caregiver$ inform* or caregiver$ train* or carer$ education or carer$ teach* or carer$ inform* or carer$ train* or Family education or family teach* or family inform* or family train*
3	Pain and physical symptoms	Pain or peripheral neuropathy or neuropathic pain or tingling or numbness Headache* or dizziness or blurred vision, seizure/tremors or symptom* or Fever or chill* or sweat* or Diarrh?ea or loose stools or nausea or vomiting or anorexia or constipation discharges or shingles/herpes zoster or rash or itching or sore* or oral throat, or painful swallowing or oral thrush, or oral candidiasis or Fatigue or muscle aches or body weakness or painful joints or Cough* or shortness of breath/ dyspn?ea or wheeze* or weight loss or swollen lymph nodes/glands or swollen feet

Table 2: Inclusion and exclusion criteria

	Inclusion	**Exclusion**
Participants	• HIV/AIDS patients of any age group. • HIV/AIDS informal caregivers (any age).	• Patients without a diagnosis of HIV/AIDS. • Informal caregivers of patients without a diagnosis of HIV/AIDS. • Paid carers such as nurses, health care assistants.
Interventions	• Any self-management intervention in line with our stated definition [40].	• Any interventions not in line with the given definition.
Studies and comparator	• Published studies written in English language only • Randomised controlled trials • Non-randomised intervention studies with a comparison group • Studies that compared one or two interventions to standard care (Intervention/s vs Standard/Usual care). Studies that compared two interventions (Intervention vs Intervention).	• Unpublished studies, studies not written in English language, conference proceedings, conference abstracts. • No comparison group.
Outcomes	• For patients: pain intensity/severity, symptom intensity/severity, pain and symptom interference with daily activities, knowledge of pain and/or symptom management, and prevalence of pain and physical symptoms, quality of life, pain and physical symptom frequency, duration and distress. • For carer participants: knowledge of pain and/or symptom management, quality of life, psychological outcomes (anxiety, stress, depression, distress) and caregiver motivation to provide care. • Costs and health service use. • Any other outcomes reported by the authors were included so long as they are in line with our inclusion and exclusion criteria.	• Outcomes not reported separately for HIV/AIDS patients and/or caregivers in studies with heterogeneous diagnostic groups

Table 3: Risk of Bias in the studies (Joanna Briggs Institute Critical Appraisal checklist) (n=19)

Yes: means good and no risk of bias, No: means there was risk of bias, ITTA: Intention to treat analysis, QoL: Quality of life.

Author	Random allocation	Allocation concealment	Baseline similarity /Comparable at entry	Blinding of participants	Blinding of those delivering treatment	Blinding of outcome assessors	Identical except intervention	Relatively complete follow-up achieved	Participants analysed in the groups originally randomised	Outcomes measures same between group	Outcomes assessed in reliable way	Statistical analysis appropriate
Parker et al, 2016	Yes	Not clear	Yes	No	No	Yes	Yes	Yes, 85%	Yes	Yes	Yes	Yes
Millard et al, 2016	Yes	Yes	Yes	No	No	Self-completed online	Yes	No, 76% completed	Modified ITTA	Yes	Yes	Yes
Millard et al, 2015	Yes	Yes	Yes	No	No	As above	Yes	No, 60% completed	Modified ITTA	Yes	Yes	Yes
Cote et al, 2015	N/A	N/A	No, traditional group had more years of formal education, better income, and married. CD4 counts were also higher	N/A	No	Self-administered	Yes	No, 55.9% completed	Modified ITTA	Yes	Yes	Yes
Nkhoma et al (2015)	Yes	Yes	Yes	No	No	Yes	Yes	Yes, 92% patients and 86%	Modified ITTA	Yes	Yes	Yes

								caregivers completed				
Webel et al, 2013	Yes	Not clear	Yes	No	No	Yes	Yes	Yes, 93% completed	Modified ITTA	Yes	Yes	Yes
Webel, 2010	Not clear	Not clear	Yes	No	No	Not clear	Yes	Yes, 80% completed	Yes, ITTA including withdraws	Yes	Yes	Yes
Wantland et al (2008)	Not clear	Not clear	No,(n=426 intervention; n=349 control)	Yes	Unclear	Self-completed by participant	Yes	No, 65.4 % completed	Yes, imputation	Yes	Yes	Yes
Chang et al (2007 a and b)	Yes	Yes	No, QoL scores were lower in the intervention	Yes	Unclear	Not clear	Yes	No, 67% completed	Yes modified and strict ITTA	Yes	Yes	Yes
Reid and Courtney (2007)	Yes	Yes	Yes	No	No	Not clear	Yes	Yes, 93.3% completed	Not clear	Yes	Yes	Yes
Vidrine et al, 2007	Yes	Not clear	Yes	No	No	Not clear	Yes	81% completed follow-up	Modified ITTA	Yes	Yes	Yes
Anastasi et al (2006)	Yes	Yes	Yes	Yes	Unclear	Not clear (nutritional assessment was conducted by nurses. Participants completed diaries.	Yes	No, 68% completed	Modified ITTA	Yes	Yes	Yes
Chiou et al (2004, 2006)	Yes	Not clear	Yes	No	No	Not stated	Yes	86% completed	Modified ITTA	Yes	Yes	Yes

Hilton et al, 2004	Not clear	Not clear	No, more male/Caucasian and gay-bisexual in the intervention	No	No	Yes	Yes	Yes, 81% completed	Modified ITTA	Yes	Yes	Yes
Pakenham et al (2002)	Not clear	Not clear	Yes	No	No	Yes, some were self-completed	Yes	Yes, 80.5 % completed	Modified ITTA	Yes	Yes	Yes
Inouye et al (2000; 2001)	Not clear	Not clear	Yes	No	No	Not stated	Yes	Yes, 97.5% completed	Described, but not clear if ITTA or modified	Yes	Yes	Not clear
van Niekerk (2000)	No	N/A	No,	No	No	Not clear	Yes	No, 67% completed	Not clear	Yes	Yes	Yes
Gifford et al (1998)	Not clear	Not clear	Yes	No	No	Self-completed	Yes	81% completed	Modified ITTA	Yes	Yes	Yes
Eller el al (1995)	Yes	Not clear	No, gender (female) differences (n=3) group1, (n=0) group2 and (n=6) group3.	No	No	Self-completed	Yes	Yes, 85.2% completed	Not stated	Yes	Yes	Yes

Table 4: Summary of GRADE in outcomes for studies reviewed

Patient outcomes							
No of studies/Design	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Number of participants in the intervention group**	**Number of participants in the control group**	**Quality**
Pain severity (follow-up period: 8-12 weeks)							
3 RCTs [82-84]	Serious[5]	No serious inconsistency	No serious indirectness	No serious imprecision	138	142	Moderate
Pain interference (follow-up period: 8 weeks)							
2 RCTs [82, 84]	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	104	105	Moderate
Fatigue (follow-up period: 6-12 weeks)							
2 RCTs [49, 83]	Serious[1]	Serious[3] inconsistency	No serious indirectness	No serious imprecision	57	59	Very low
Diarrhoea (follow-up period: 3-24 weeks)							
1 RCT [85]	No serious	No serious inconsistency	No serious indirectness	Serious[4]	38	37	Moderate
Weight loss/gain (follow-up period: 10-16 weeks)							
1 RCT [86]	Serious[1]	Serious[3] inconsistency	No serious indirectness	Serious[4] imprecision	15	15	Very low
1 Non-RCT[87]	Very serious[6]	Very serious[7] inconsistency	No serious indirectness	Serious[4] imprecision	60	30	Very low
Physical symptoms (follow-up: period 6-24 weeks)							
7 RCT [54, 59, 62, 64, 65, 83, 88]	Serious[1]	Serious[3]	No serious indirectness	No serious imprecision	668	593	low
1 Non-RCT [89]	Very serious[2]	Serious[3]	No serious indirectness	Very serious[8]	99	80	Very low
Quality of life (follow-up period: 7-16 weeks)							
9 RCT [54, 57, 62, 64, 65, 69, 82, 90, 91]	Serious[1]	Serious[3]	No serious indirectness	No serious imprecision	354	355	low
Knowledge (follow-up period: 8-16 weeks)							
6 RCT [54, 57, 64, 82, 83, 92]	Serious[1]	Serious[3]	No serious indirectness	No serious imprecision	246	243	low
Caregiver outcomes							

[5] No blinding of participants and those delivering the intervention
[6] No randomisation
[7] Clinical heterogeneity, methodological heterogeneity (use of tools without established psychometric properties)
[8] High attrition rate, few participants analysed, small sample size

Quality of life (follow-up period: 8 weeks)							
2 RCT [64, 82]	Serious[1]	No serious inconsistency	No serious indirectness	No serious imprecision	104	102	moderate
Knowledge (follow-up period: 8 weeks)							
2RCT[64, 82]	Serious[1]	Serious[3]	No serious indirectness	No serious imprecision	104	102	low

Table 5: Characteristics of studies included for patient participants (n=17 studies)

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Parker et al (2016), South Africa	Evaluate a peer-led exercise and education intervention on pain among women with HIV RCT Bio-psychosocial model	N=27 participants (all female) n=12 intervention n=15 control Mean age 30.8(SD=4.5) years.	A 6 week, 2 hourly peer-led exercise and education programme. Covered self-management of pain and physical symptoms. Also received workbook developed for the intervention. Comparison group received usual care consisting of routine attendance at the clinic for monitoring monthly or three monthly. Workbook developed for the intervention and a pencil.	Primary outcome: 1.Pain severity: BPI-Xhosa Secondary outcome: 2.Pain interference: BPI-Xhosa 3. QoL: Health related QoL (EQ-5D Xhosa). Data collected at weeks 0, 4,8,12 and 16	1. No significant differences (f=0.93, p=0.46). 2. No significant improvement (f=0.2, p=0.98). 3. No significant differences (f=0.36, p=0.87).
Millard et al (2016), Australia	Evaluate the effectiveness of an online self-management programme in improving health outcomes and well-being for gay men with HIV. RCT. Bandura's self-efficacy theory	N=132 participants (gay men) n=68 intervention n=64 control Mean age 42.3(SD=10.4) years.	Positive outlook programme using self-management approach to manage psychosocial aspects of HIV in daily life, consisting of information, action planning activities, discussions. Peer-led delivered online 90 minutes per week for seven weeks. Comparison group received usual care including primary health and community based services and support.	Primary outcomes: 1.QoL/Physical health and symptoms: Patient Reported Outcomes QOL-HIV(PROQOL-HIV)	1. Significant improvements were seen in the following PROQOL-HIV subscales (group by time interaction p value): body change (p=0.036), social relationships (p=0.035), emotional distress (p=0.031). Baseline vs 8 weeks: body change p=0.089, social relationships p=0.051, emotional distress (p=0.017) Baseline vs 12 weeks: body change (0.020), social relationships (0.047), emotional distress (p=0.269).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
				2.Health Education Impact: Health Education Impact Questionnaire (HEIQ)	2. Intervention showed significant improvements in HEIQ subscales (group by time interaction p value): health directed activity (p=0.048), constructive attitudes and approaches (p=0.015), skill and technique acquisition (p=0.046), health service navigation (p=0.008). Baseline vs 8 weeks: Health directed activity (p=0.289), constructive attitude approaches (p=0.026), skill technique acquisition (p=0.044), health service navigation (p=0.018). Baseline vs 12 weeks: Health directed activity (p=0.014), constructive attitude approaches (p=0.757), skill technique acquisition (p=0.834), health service navigation (p=0.915).
				3. Self-management skills: HIV specific self-efficacy measured by a Positive Outlook Self-Efficacy Scale (POSE) developed for this study.	3. Intervention group improved significantly on self-management skills, POSE (group by time interaction p value): relationships (p=0.019), social participation (p=0.006) and emotions (p=0.041).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
				Measured at baseline, 8 weeks and 12 weeks.	Baseline vs 8 weeks: relationships (p=0.010), social participation (p=0.004) and emotions (p=0.049). Baseline vs 12 weeks: relationships (p=0.126), social participation (p=0.432) and emotions (p=0.731).
Millard et al (2015), Australia	To assess the feasibility, acceptability and effectiveness of positive outlook online self-management programme for gay men with HIV/AIDS. RCT. Bandura's self-efficacy theory	N=35 participants (gay men) n=17 intervention n=18 usual care. Mean age 41.54(SD=9.83) years.	As above (The intervention is the same, but participants recruited were different)	As above. Assessments conducted at baseline and 8 weeks	1.PROQoL: No significant differences between groups (P=0.58) 2. No significant differences (p=0.96) 3.total scores were not significant (p=0.78) Authors report that this trial was not powered to detect statistical significant differences.

Author/Country year	**Aim** **Design** **Theoretical model**	**Sample**	**Intervention(s)**	**Outcomes/measures and follow-up period**	**Results**
Cote et al (2015), Canada.	Comparing the effectiveness of a traditional and virtual intervention in promoting self-management of HIV treatment. Quasi-experiment study. Bandura's self-efficacy theory.	N=179 HIV participants. n=99 were recruited at a site offering virtual follow-up care. Mean age 47(SD=7.6) years. Male gender n=82(82.8%). n=80 at a site offering traditional care. Mean age 49(SD=9.2) years. Male gender n=71(88.8%).	HIV treatment, Virtual Nursing Assistance and Education which consisted of four interactive computer sessions, each 20-30 minutes, engaging patients in a self-management skills process. Provided over 8 weeks period. Session 1 focuses on self-assessment skills, session 2 emotional management, session 3 focused on how to establish, maintain, and strengthen social relations and interact with health professionals, session 4 consolidation of all the skills above. Comparison group received traditional care consisting of meeting health care professionals over a period of 3 to 4 months, lasting 20 minutes which covers medication, symptoms, and problems encountered.	Primary outcome: 1. Adherence: 7 item questionnaire to measure how often a person forget to take medications. Secondary outcome 2. Symptom related discomfort: 20 item-Self completed HIV Symptom Index. Assessments were conducted at baseline, 3 and 6 months.	1. Adherence was high at baseline (virtual vs traditional) 84% vs 80%, at 3 months adherence was 90.4% vs 86%, at 6 months 90% vs 93%. (Z=-1.36, p=0.174). 2. Symptom bother (F=0.562, p=0.46).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Webel et al (2013), USA.	To evaluate the feasibility and estimate the magnitude of the effect of a behavioural intervention (systemCHANGE), on sleep outcomes and quality of life among adults with HIV/AIDS. RCT.	N=43 n=21 intervention. Mean age 49.1(SD=7.4) years. n=22 control. Mean age 47.8(SD=6.4) years. (Nine females each group).	SystemCHANGE, consisted of 10 weekly sessions on HIV management, sleep hygiene, and behavioural modifications which affect health. Participants were encouraged to attempt small tests of change and modify the changes for the benefit of self-management of HIV sleep related problems. Facilitated by educator or registered nurse. Comparison group received a copy of HIV Symptom management strategy [59].	Primary outcomes: 1. Sleep duration and quality: Wrist actigraphy. Participants wore an actigraph continuously for one week at baseline and at 10 weeks later, sleep fragmentation index and sleep efficiency. Sleep disturbances and sleep impairments: Patient Reported Outcomes Measurement Information (PROMIS) Sleep. Disturbance and Sleep-Related Impairment Scales. Secondary outcome: 2. QoL: HIV/AIDS Targeted Quality of Life Instrument-34. Follow-up at week 10.	SystemCHANGE participants experienced 10 minute night increase in sleep time (t=0.39; P=0.71), 2.3% increase in sleep efficiency (t=0.98; p=0.33), 2% decrease in sleep fragmentation (t=0.58; P=0.57), 0.7 decrease in sleep disturbances (t=-0.27; p=0.79) and 0.5% -point increase in sleep-related impairments (t=0.16; p=0.88) compared to the control group. Furthermore systemCHANGE participants experienced a 2.1 point increase in life satisfaction (t=0.28; p=0.79) and 3 point increase in overall functioning (t=0.58; p=0.57) compared to the control group. 2. QOL overall functioning: 3.6(-6.7,13.8) p=0.49. QOL satisfaction: 1.7(-13.1, 16.6) p=0.81.

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Webel (2010), USA	Evaluating the impact of a peer-based symptom management intervention for women with HIV/AIDS. RCT.	N=89 women n=43 intervention. Mean age 48 (27-67) years n=46 control. Mean age 45.9 (31-72) years.	HIV symptom management: positive self-management programme [83]. Seven interactive health education group sessions on self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition facilitated by three peer leaders. Comparison group received a copy of HIV Symptom management strategy [59].	Primary outcomes: 1. Symptom intensity: HIV sign and symptom checklist-revised; 72 most common symptoms. 2. QoL: HIV Targeted Quality of Life Instrument, a 34-item disease-specific instrument measuring nine dimensions of QoL. 3. Medication adherence: Revised AIDS Clinical Trials Group (ACTG), Reasons for Non-Adherence to Medications (ACTGrev). Assessments were conducted at baseline, week 2, week 6, week 10, and week 14.	1.The mean total symptom intensity was not significantly difference between the PSMP and the symptom manual group -0.13(SD=027); p=0.94) 2. No significant differences on QoL between the PSMP and manual groups - 0.66(SD=4.87); p=0.99). 3. No significant differences on adherence, mean - 0.13(SD=0.428; p=0.207).
Wantland et al (2008), Kenya, South Africa, Puerto Rico, and USA.	Efficacy and helpfulness of the self-care symptom management manual compared to the general nutrition based manual. RCT.	N=775. Mean age 42.8 (SD=9.6) years. Female gender n=296 (38.5%). n=426 intervention n=349 control	Experimental group received a manual on symptom management. Comparison group received a manual on general nutrition in HIV/AIDS.	Primary outcome: 1. Frequency and intensity of HIV symptoms: Revised Sign and Symptom Checklist for persons with HIV disease (SSC-HIV). Secondary outcome: 2. Frequency of use of the manuals and perceived helpfulness: The Symptom and Nutrition Helpfulness Assessment Tool. Measures administered at baseline, one month and two months follow-ups.	1. There was a greater decline in symptom frequency and intensity for the experimental group compared to the control group (t=2.36, P=0.018). 2. Symptom manual was significantly more useful/helpful at one month (t=3.27, p<0.001) and two months (t=3.15, p=0.002). The symptom manual was significantly more frequently used at one month (t=3.23, P=0.002), and two months (t=3.18, p<0.002).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Chang et al (2007a and b), (Two papers reporting one study), USA	Evaluate the effects of adding relaxation response (RR) to usual acupuncture treatment on QoL among HIV/AIDS patients. RCT.	N=119 n=58 intervention. Mean age 45.5 (SD=7.3). Male gender n=49 (84%). n=61 control. Mean age 45.5 (SD=7.8). Male gender n=52 (85%)	Listened to tapes which contained relaxation response (RR) techniques during acupuncture treatment and twice daily at home. Comparison group listened to tapes with soft music (without RR) during acupuncture treatment using earphones. The music was routinely played in the clinic. They did not listen to tapes at home.	Primary outcome: 1. Changes in symptoms, emotions, response to stress. Secondary outcomes: 2. Health-related QoL: Medical Outcomes Study (MOS-HIV), Functional Assessment of HIV Infection (FAHI), and Functional Assessment of Chronic Illness Therapy-Spiritual Well-Being (FACIT-Sp). 3. Experience of listening to tapes at the clinic Outcomes for (1) were conducted at baseline, weeks 4, 8, and 12, for (2) at baseline and 12 weeks.	1. RR group reported emotional, physical and spiritual (46% vs 21%) improvement, including feeling peaceful, relaxed and calm (30% vs 26%) compared to the music group (p=0.02). 2. Group differences were not statistically different even though there was a trend towards greater improvement at 12 weeks in all scores in the intervention group compared to the control group. 3. RR group reported a better experience with the tapes compared to the music group (p=0.056).
Reid and Courtney (2007), Australia	To evaluate the effects of diet programme on weight loss and ways of coping among people living with HIV and lipodystrophy. RCT.	N=30 men n=15 intervention. Mean age 45.79 (SD=9.94) years, n=15 control. Mean age 48.2 (SD=8.59).	Self-management diet programme consisting of 4 visits to the dietician (at 0, 2, 6 and 10 weeks), to provide support monitoring programme implementation. Information booklet about diet. Comparison group received the diet programme and information booklet at the end of the study.	Primary outcome: 1.Weight loss: Impact of Weight Loss Scale 2.Ways of coping: Ways of coping questionnaire Outcomes assessed at baseline and at week 10.	The intervention group showed significant positive feelings about loss weight compared to the control (p=0.04) 2. The scores intervention showed nonsignificant improvement compared to the control group (p>0.05).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Vidrine et al, (2007), USA	Examining the effects of changes in smoking status on HIV-related symptom burden and health-related quality of life outcomes. RCT.	N=95. Mean age 43.5(SD=7.8) years. n=48 intervention. Mean age 42.6 (SD=8.2) years. Male gender n=35 (72.9%). n=47 control, mean age 43.1 (SD=8.1) years. Male gender n=39 (83%).	8 proactive counselling sessions via cell phone and access to hotline including usual care. Usual care: Comparison group received brief advice to quit smoking, 10-week prescription of nicotine replacement therapy and self-help written materials.	Primary outcome: 1. HIV/AIDS related symptom status: 20-item measure of symptom frequency and burden. Secondary outcomes: 2. Smoking status: point prevalence abstinence and length of smoking abstinence. 3. Health related QoL: Medical Outcomes Study (MOS-HIV). Outcomes were assessed at baseline and 3 months.	1. Longer length of abstinence was significantly associated with low symptom burden (p=0.02). 2. Cell phone participants were significantly more likely to abstain from smoking compared to usual care participants (37% vs 10.3%, x^2 =7.6 p=0.006). Cell phone participants reported a significantly longer period of abstinence compared to usual care participants: 31 days vs 12 days, t=3.12, p=0.003. There was a higher proportion of participants who made attempt to quit smoking in the cell phone group (97.4%) compared to (74.4%) in the usual care group: X^2=8.32, p=0.004. 3. Abstinence was not associated with physical health status (p=0.93) and mental health status (p=0.18).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Anastasi, et al (2006, USA.	Evaluate the efficacy of a dietary intervention to reduce the frequency of bowel movements and improve stool consistency. RCT. The theory of planned behaviour and theory of reasoned action.	N=75 with HIV related diarrhoea. Mean age 43.5 (SD=10.1) years. Male gender n=53 (70.7%). n=38 intervention. Male gender n=25 (65.8%). n=37 control. Male gender n=28 (75.7%).	Instructed to eat a low fat, lactose free, low insoluble fiber, high soluble fiber, and caffeine-free diet. Preparation of tasty foods in line with the diet, strategies to keep the diet cost-efficient. Comparison group were provided with standard information on safe-care and healthy living with HIV-AIDS, without information about diet, and received the intervention after completion of the study. Both groups attended six study sessions.	Primary outcomes: Food and stool diary: participants recorded food intake, stool frequency, stool consistency, and ant-diarrhoea medication in a food and stool diary every day. Measures conducted at baseline, 3 weeks and 24 weeks.	After 3 weeks the average daily stool frequency was significantly lower in the intervention group compared to the control group (F=5.57; P=0.006). After 3 weeks the average daily stool consistency significantly improved in the intervention compared to the control (F=8.92; P=0.0003). Stool frequency further reduced at 24 weeks in the intervention group compared to the control group (F=9.22; P=0.0003). Stool consistency also improved in the intervention group compared to the control group (F=9.98; P=0.0002).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Chiou et al (2006; 2004) (Two papers reporting one study), Taiwan	Evaluation of the effects of a symptom management programme on drug adherence, CD4count viral load and quality of life of patients with HIV/AIDS. RCT. Heinich's model.	N=67 n= 23 individual teaching, mean age 31.17 (SD=5.62), male gender n=22 (95.7%) n=22 group teaching, mean age 34.27 (SD=7.67), male gender n=20 (90.9%) n=22 usual care, mean age 31.91 (SD=6.52), male gender n=21 (95.5%).	(1) Individualised (one-to-one teaching): attended a 60-90 minute teaching programme on antiretroviral (ART) side effects, safe-care education and skill training (manual-based) weekly, for 3 weeks and telephone counselling anytime during the research to discuss the education and skill manual. (2) As above, but was group-based. (3) Comparison group received usual care (details not provided), and received the intervention after conclusion of data collection	Primary outcomes: 1. Adherence: Customised adherence self-report (CASQ). 2. Medication side-effects self-care knowledge: assessed with medication side effects self-care knowledge questionnaire (MSSKQ)-20 item (higher scores better outcomes). 3. Immune system: CD4 count and viral load.	1. Median adherence difference was 5.03 % (IQR=3.20) in group1, and 6.19(IQR=3.65) in group2, compared to 1.42 %(IQR=9.20) in the control group. (Kruskal Wallis p=0.030). 2. 'Both teaching/intervention groups showed significant improvement in self-care knowledge in managing side effects from medication compared to the control group' (Kruskal Wallis test P<0.001). Mean MSSKQ was 8.26(SD=2.94) higher in the individual group (z=-4.209; p<0.001); Mean MSSKQ was 8.41(SD3.63) higher in the group intervention (z=-4.114, p<0.001). Mean MSSKQ was 0.73(SD=2.29) higher in the control group (z=-1.548, p=1.22). Kruskal Wallis test (p<0.001). 3. Median CD4 count difference 37.09 mm^3 (IQR=69.01) (z=-2.017, p<0.05) in group1, and 39.98 mm^3 (IQR=63.88) (z=-1.988,p<0.05) in group2 compared to -7.46 mm^3 (IQR=42.01) (z=-0.474, p=0.636) in the control group. (Kruskal-Wallis P<0.05). Median viral load difference was -14613/mL (IQR=52357) (z=-2.456,p=0.014) in

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
					group1, and -11779/mL (IQR=32143) (z=-2.840, p=0.005) in group2 compared to -575.46/mL (IRQ=1431) (z=-1.084, p=0.297) in the control group. (Kruskal-Wallis P<0.05).
				4. Quality of life (QOL) measured using QOL index, evaluated after three months.	4. QOL in both experimental groups were statistically significantly better median difference 1.20(IQR=0.50) (z=-2.858, P=0.004) in group 1, and 1.43(IQR=0.45) (z=-2.160, P=0.031) in group 2 compared to the control group -0.32(IQR=0.05) (z=-0.666, P=0.506). Kruskal-Wallis test (P=0.011).
				5. Self-Esteem: Rosenberg's Self-Esteem Scale (RSES)-10 item	5. Mean RSES: 0.261(SD=3.77) in the individual group (z=-0.899, p=0.369). Mean RSES: 0.682(SD=3.60) in the group intervention (z=-0.525, p=0.599). Mean RSES: -0.045(SD=2.80) in the control group (z=-305). No significant differences between groups (Kruskal-Wallis test, p=0.650).
				6. Unscheduled hospital visits: recording planned visits and comparing with unplanned.	6. At follow-up mean Unscheduled hospital visits (UHV): -0.48(SD=0.85) in the individual group (z=-2.39, p=0.017), and -0.36(SD=0.79) in the group intervention (z=-2.111,

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
				Assessments conducted at baseline and follow-up at three months.	p=0.035). Mean UHV: -0.045(SD=0.49) in the control group (z=-0.447, p=0.655). Both interventions significantly reduced unscheduled hospital visits (p<0.05).
Hilton et al, 2004, USA	To evaluate the efficacy of a behavioural self-care intervention programme to reduce oral thrush in HIV infection. RCT.	N=35 participants with oral candidiasis n=18 intervention, mean age 48.4 (SD=6.2) years. Male gender 83.3%. n=17 control, mean age 44.9 (SD=6.8) years. Male gender 64.7%.	24 hour diet recall and oral hygiene diary at every follow-up visit (2-3 weeks for 6 months). Dentist provided advice on how to modify eating and oral hygiene to reduce exposure to exogenous sugars. Dietary advice to prevent dental caries, reduce duration and frequency of eating, eliminate between meal sugary snacks, and perform oral hygiene after each meal. Instructed to brush (2 minutes), floss (first and last time they ate for the day) and rinse the mouth thoroughly. Handouts were provided. Oral hygiene aids were provided. Taught oral self-examination.	Primary outcomes: 1. Risk of recurrence. Secondary outcomes: 2. Performing oral hygiene after meals/snacks. 3. Self-diagnosis of oral thrush. 4. prevalence of candidiasis at follow-up	1. Candidiasis recurrence at 6 months was 78% in the intervention, and 88% in the control (hazard ratio 0.72, 95% CI 0.35 to 1.50; P=0.37). 2. Oral hygiene greatly increased in the intervention by 26-32% compared to increase by 2- 19% in the control. 3. No differences between the intervention and control groups. 4. 26% in the intervention and 31% in the control (odds ratio 0.76, 95% CI 0.35 to 1.61; P=0.47).

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
			Comparison group received 24 hour recall diet hygiene diary at the first and last follow-up visits only. No advice was provided.	Assessments conducted at baseline and 6 months follow-up.	
Inouye, et al (2000, 2001). (Two papers reporting one study), USA	To assess the effects of self-management on various measures of health and well-being of PLWH. RCT. Social learning and cognitive theories	N=40. Mean age 37 (25-53) years, two in each group were females. (n=20 per group).	Individualised, 7 week group-based programme of self-management training and education sessions (60-90 minutes) provided twice per week, facilitated by two clinicians. The sessions included biofeedback-assisted relaxation techniques of imagery, abdominal breathing, progressive muscle relaxation, and autogenic training. Coping strategies included cognitive restructuring and management of stressful emotions such as anger, depression, anxiety, and problem-solving skills. Comparison group received usual care provided by primary care providers (details not provided). At follow-up watched a video about nutrition in HIV/AIDS and received a shorter version of the intervention in groups including resource materials.	Primary outcomes: 1. Quality of life (QOL): quality of life index (QLI)-34 items. Secondary outcomes: 2. Physical health status: number of physical symptoms (self-report from symptom checklist), Physical functioning: Karnofsky Performance Status Scale (KPS), and CD4 count. 3.Attitudes about health: Health Attribution Test (HAT) Outcomes conducted at baseline and after seven weeks.	1. No significant effects on quality of life. Overall intervention showed 5.75% increase in their QOL, compared to 0.39% decrease for control participants. Participants with high symptoms showed better improvement compared to participants with low symptoms. 2. No significant differences on mean number of symptoms (M=7.2; intervention vs M=9.0, control; P>0.05). KPS scores (M=87.5; intervention vs 88.6 control; P>0.05). Mean CD4 count P>0.05). 3. Health attribution significantly improved (F=4.50; p<0.05).
van Niekerk, et al, (2000) South Africa	The effects of nutritional education and dietary counselling on body weight among HIV/AIDS participants not on HAART	N=90 seropositive, but not on HAART. Mean age 33 (19-68) years. Female gender n=63 (70%).	Nutritional education and diet counselling by dietician. Dietary guidelines according to identified problems (anorexia,	Primary outcome: 1. Body weight.	1. Body weight was significantly greater in the intervention group compared to the control group (P<0.01). Weight gain occurred in 53% in the intervention

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
	Matched control design	n=60 intervention, n=30 control.	weight loss, nausea/vomiting, oral pain and other symptoms). No details provided for comparison group.	 Secondary outcome: 2. incidence of opportunistic infections Mean follow-up period was 4.2 months, mean number of visits, 3.	(mean=3.5kg) compared to 21% in the control (mean=2kg); P<0.03. Weight loss was seen in 27% in the intervention group compared to 43% in the control group. 2. The incidence of opportunistic infections in those who lost weight was 88%, where as those who maintained or gained weight was 45%. The intervention appeared to be associated with less opportunistic infections (67% had opportunistic infection in the diet intervention, compared to 78% in the control group).
Gifford et al (1998), USA	Evaluate the acceptability, practicality, and short-term efficacy of a health education programme to improve disease self-management in patients with symptomatic HIV/AIDS. RCT. Bandura's self-efficacy theory	N=71 gay men n=34 experimental group, mean age 45.2 (SD=9.4) years; n=37 control group, mean age 45.3 (SD=8.1) years.	Positive Self-Management Programme (PSMP) 7 interactive health education group sessions on self-management skills and information on symptom assessment and management, medication use, physical exercise, relaxation, communication with doctor and nutrition facilitated by 2 peer leaders. Control group received usual care, and received the intervention after follow-up assessments.	Primary outcomes: 1. Symptom severity assessed with a 14-item symptom severity index (created by authors). 2. Pain was assessed with 5-item Medical Outcomes Study. 3. Fatigue: 8-item subscale from a profile of mood state. Secondary outcomes: 4.Physical exercise, stress management and HIV/AIDS	1. Symptom severity decreased in the experimental group and increased in the control group (-0.9 versus +0.5; p <.03). 2. There were no significant differences in pain outcome between the intervention and control. 3. Mean fatigue score showed no significant difference between the intervention and control group. 4. There were no significant differences in physical exercise (p=0.06), stress

Author/Country year	Aim Design Theoretical model	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
				Knowledge: total time spent on exercises/relaxation techniques, and 10 item knowledge questionnaire Outcomes conducted at baseline and 3 months after randomisation.	(p=.48) and knowledge (p=0.17).
Eller, (1995), USA	To evaluate the effects of a guided imaginary, or progressive muscle relaxation (PMR) on fatigue, depression and immune status among HIV/AIDS participants. RCT.	N=69 n=23 group 1, mean age 33.6 (SD=6.2) years. Male gender n=20 (87%) n=22 group2, mean age 36.5 (SD=6.3) years. Male gender n= 22 (100%) n=24 group 3, mean age 39.0 (SD=11.9) years. Male gender n=18 (75%).	(1). Guided imagery treatment, 21.5 minute audio visual tape delivered in a female voice and used daily for 6 weeks. Contained instructions for slow, and deep breathing. Images focused on desired changes in immunity, fatigue and depression. (2). Progressive muscle relaxation (PMR), 12 minute audio tape in female voice used daily for six weeks. Consisted of instructions on systematic tensing and relaxation of muscle groups. Both 1 and 2 were instructed to use the audiotapes daily and record the frequency of use in a logbook at home. They were allowed to call should they have any questions. (3). No details provided for comparison group but received the cassette and headphones upon completion of the study.	Primary outcome: Fatigue: Rest and sleep subscale of the Sickness Impact Profile Outcomes conducted at baseline and six weeks	Guided imagery demonstrated a decrease in fatigue (Mean change 16.8 (SD=17.39) to 11.6 (SD=12.89) P=0.04, PMR and control groups failed to demonstrate decrease in fatigue 12.18 (SD=13) to 12.44 (SD=12.09), (P=40).Control group (Mean 18.29 (SD=15.29) to 18.9 (SD=16.85).

Table 6: Characteristics of studies included for patient and caregivers participants (n=2)

Author/Setting	Aim/design	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Nkhoma, et al (2015), Malawi	To evaluate the effects of a pain educational intervention on pain severity and pain related outcomes among patients with HIV/AIDS and their family carers. RCT. bio-psychosocial model	N=182 patients/carer dyads N=92 pain education. For patient participants: Mean age 40.5 (SD=11.3), female gender n=49 (53.26%). For caregivers participants: Mean age 41.1(SD=11.7), female gender n=76 (84.44%) N=90 usual care. For patient participants: Mean age 41.3 (SD=11.65), female gender n=34 (37.78%). For caregivers participants: Mean age 42.6(SD=11.4), female gender n=71 (78.89%).	Nurse led-pain education intervention consisting of: (1) information leaflet (2) 30 minutes face-to-face discussion (3) phone call reminder among HIV/AIDS patients/carers dyads. Comparison group received care consisting of access to care provided by staff members, routine medical appointments and leaflet after follow-up assessments.	Primary outcomes: 1.Pain severity: The Brief Pain Inventory (BPI-PS) Secondary outcomes: 2. Pain interference: The Brief Pain Inventory (BPI-PI). 3. Patient pain knowledge: Patient Pain Questionnaire (PPQ-K) 4. Patient quality of life: African Palliative Outcomes Scale (APOS). 5. Carer pain knowledge: Family Pain Questionnaire (FPQ-K) 6. Carer quality of life: African Palliative Outcomes Scale (APOS) 7. Carer motivation: Picot Caregiver Rewards Scale (PCRS). Assessments were conducted as baseline and follow-up at week 8 (2 months).	1-4: Patients experienced a significant improvement in all outcomes (pain severity, interference, knowledge and QoL)(P<0.001) 5-7: Carers experienced a significant improvement in all outcomes (Knowledge, QoL and motivation) (P<0.001).

Author/Setting	Aim/design	Sample	Intervention(s)	Outcomes/measures and follow-up period	Results
Pakenham et al (2002), Australia	To evaluate the efficacy of a psychosocial intervention for caregivers and patients with HIV/AIDS. RCT.	36 caregivers and care-recipients with HIV/AIDS n=12 group1. For patient participants: Mean age 35.45 (SD=7.05) For caregivers: Mean age 35 (SD=9.19), male gender n=8 (73%). n=12 group2. For patient participants: 34.88 (SD=8.79) For caregivers: Mean age 41.50 (SD=13.31), male gender n=5 (63%) n=12 group3. For patient participants: Mean age 34 (SD=9.96) years, For caregivers: Mean age 45.4 (SD=12.6), male gender n=6 (60%).	(1) Dyad intervention (DI) caregivers and their patients: eight weekly sessions of one and half hours conducted by psychologists. Based on two HIV target problems which participants stated (2) Caregiver Intervention (CI) caregivers only: intervention as above. (3) Comparison group received standard care (details not provided). They were on wait list control (WLC) that is, they received the intervention after follow-up assessments.	1. Global distress: The Brief Symptom Inventory (BSI). 2.Subjective health status: Global Rating of Health Scale. 3.Social adjustment: The Psychosocial Adjustment to Illness Scale. 4. Target problem 1 and 2. (outcomes assessed at 0,2 and 4 months)	1-Caregivers in the DI group improved significantly compared to CI and WLC on global distress, $t(10)=2.70;P<0.01$. 2-Both cares in the CI and DI groups improved significantly on subjective health status $t(10)=5.16$; $P<0.001$ and $t(7)=3.74$; $P<0.01$ respectively compared to the WLC group. 3- Carers in all the three groups improved on social adjustment, $F(1, 26) =39.90$, $P<0.000$, $n^2=0.61$. 4.DI group showed significant improvement in target problems compared to CI and WLC ($p<0.01$) Care recipients in the DI group improved significantly on social adjustment ($t(9) =5.71$; $P<O.001$) and subjective health status ($t(9) =3.00$; $p=0.01$) outcomes compared to care recipients in the CI and WLC groups. Care recipients in all the three groups improved on global distress $F(1,25)=4.48$; $P<0.05, n^2=0.15$ DI showed a significant improvement in target problems compared to CI group ($p<0.001$)

Table 6: JBI Critical Appraisal Checklist for Randomised Controlled Trials

Item No.	Checklist item	Yes	No	Unclear	NA
1	Was the assignment to treatment groups truly random?				
2	Was allocation to treatment groups concealed?				
3	Were treatment groups similar at baseline				
4	Were participants blind to treatment assignment?				
5	Were those delivering treatment blind to treatment assignment?				
6	Were outcome assessors blind to treatment assignment?				
7	Were treatment groups treated identically other than the intervention of interest?				
8	Was follow-up complete, and if not, were strategies to address incomplete follow-up utilised?				
9	Were participants analysed in the groups to which they were randomised?				
10	Were outcomes measured in the same way for treatment groups?				
11	Were outcomes measured in a reliable way?				
12	Was appropriate statistical analysis used?				

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