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School of Health Related Professions



**HIV Disease and Distal Sensory Polyneuropathy (DSP)**

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**BACKGROUND**

- Studies of patients with HIV disease have reported neuropathy prevalence ranging from 38% to 53%.<sup>1-4</sup>
- Individuals with HIV-related DSP typically experience pain, numbness, paresthesia, reduced quality of life compromised function, and episodic disability.<sup>5-6</sup>

1. deCossa DB, Boreventura M, et al. The association of HIV/AIDS treatment side effects with health status, work productivity, and resource use. *AIDS Care*. 2012;24(8):744-755.  
2. Ellis RJ, et al. Continued high prevalence and adverse clinical impact of human immunodeficiency virus-associated sensory neuropathy in the era of combination antiretroviral therapy: the CHARTER Study. *AIDS Readout*. 2010;6(7):552-558.  
3. Sridharan S, Rhoads. Peripheral neuropathy and quality of life of adults living with HIV/AIDS in the Florida district of Nevada. *Saunders*. 2009;20(2):88-94.  
4. Nicholas et al. Prevalence, self-care behaviors, and self-care activities for peripheral neuropathy symptoms of HIV/AIDS. *Nursing & Health Sciences*. 2010;12(1):119-126.  
5. Dixon S, Chantarat A, Jansen JP. Epidemiology of HIV-related neuropathy: A systematic literature review. *AIDS Research and Human Retroviruses*. 2012; 28(1): 36-48.  
6. Hickey A, Corbridge DR. Peripheral neuropathies in human immunodeficiency virus infection. *Support Care Oncology*. 2004; 12:156-210.

Tool	Psychometric Properties	Description
<b>Total Neuropathy Score</b>	Validated in patients with chemotherapy-induced neuropathy and diabetic neuropathy Inter-rater reliability: .866 Intra-rater reliability: .866	Overall score with range of 0-32 points Components: grading of sensory, motor, and autonomic symptoms pin & vibration sensation strength tendon reflexes electrodiagnostic tests: sensory nerve amplitude peroneal nerve amplitude
<b>Subjective Peripheral Neuropathy Screen</b>	Validated in patients with HIV-related DSP Reliability: .86 Specificity: 84% Sensitivity: 51% Diagnostic Efficiency: 69%	6 questions related to presence and severity (0-10 scale) of: pain, itching, burning pins and needles numbness
<b>Brief Peripheral Neuropathy Screen</b>	Validated in patients with peripheral neuropathy Specificity: 98% Sensitivity: 49% Diagnostic accuracy: 78%	2 questions regarding DSP symptoms (pain/itching/burning; pins and needles; numbness) 2 clinical tests: vibration sensation test (120Hz tuning fork) Achilles tendon reflex +DSP if one or more symptoms AND either diminished vibration sensation or diminished Achilles' reflex
<b>Neuropathy Severity Score</b>	Validated in patients with HIV-related DSP Specificity: 91.7% Sensitivity: 66.7%	6 questions 2 questions related to symptom (pain/itching/burning; pins and needles; numbness) severity 3 questions related to function 1 clinical test: Achilles' tendon reflex
<b>Single Question Neuropathy Screen</b>	Specificity: 86% Sensitivity: 95.7%	1 question: "Do you experience tingling, burning, or numbness in your feet and hands?"

**Screening Tools for DSP Associated with HIV Disease<sup>1,2</sup>**

1. Galantino et al. Screening tools for distal sensory peripheral neuropathy associated with HIV disease. *Rehabilitation Oncology* 1(1), 10-23, 2013.  
2. Galantino et al. Screening tools for distal sensory peripheral neuropathy associated with HIV disease. Poster presented at the 4<sup>th</sup> International Workshop on HIV Disease and Aging, Baltimore MD, Nov. 2013.

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**Other Screening and Assessment Tools for DSP<sup>1</sup>**

- Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)**
  - Combo of physical exam signs and patient symptom self-report
  - Sensitivity 82%; specificity 80%
- Neuropathic Pain Questionnaire (NPQ)**
  - 12 numerical scale questions; formula derived score: Positive score predicts presence of neuropathic pain (sensitivity 67%; specificity 71%)
- Douleur Neuropathique 4 Questions (DN4)**
  - Combo of physical exam and self-report of symptoms: Score of 4 (out of 10) or higher identifies neuropathic pain (specificity 83%; sensitivity 90%)
- painDETECT**
  - 7 item self-assessment tool (score >19 =neuropathic pain: sensitivity 85%; specificity 80%)
- ID Pain**
  - 6 yes/no questions (score >=2 =neuropathic pain: sensitivity 73%; specificity 69%)
- Standardized Evaluation of Pain (SEP)**
  - Combo of symptoms and exam signs, validated for pts with neuropathic low back pain
- Neuropathic Pain Scale**
  - 7 numerical scale questions; used in studies examining effectiveness of pain treatments
- Neuropathic Pain Symptom Inventory (NPSI)**
  - 12 numerical scale questions; used to assess efficacy of pain treatment and characterize symptoms
- Short Form McGill Pain Questionnaire 2 (SF-MPQ-2)**
  - Items divided into 4 descriptor subscales; used to characterize chronic pain and measure response to treatment

1. Jones RC & Backinger M. Review of Neuropathic Pain Screening and Assessment Tools. *Current Pain and Headache Reports* 17(7):383, 2013.

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**Physical Therapy and Acupuncture for HIV Associated Distal Sensory Polyneuropathy (DSP): A Systematic Review<sup>1</sup>**

**Summary of Acupuncture Studies**

Author	Study Design	Intervention(s)	Outcomes	Time(s) to Outcomes	Key Findings	Level of Evidence
Shay et al. (2005)	RCT N=250	14 weeks of: Acupuncture Antidepressive Acupuncture + Antidepressive Placebo (control acupuncture points)	Mean pain score (Dorothy scale) Global rating of pain relief Neurologic Summary Score Quality of life	6 weeks 18 weeks	No significant between group differences in any outcome measure	2b
DuFrenoy & Silveira (2010)	Re-analysis of subset of data from Shay et al. (2005) N=121	As above	Mean pain score (Dorothy scale) Global rating of pain relief Attrition Mortality	6 weeks 18 weeks	Lower pain intensity and greater pain relief in acupuncture group. OR acupuncture group compared to combination or compared to placebo Reduced attrition in acupuncture group Lower mortality in acupuncture group	3
DuFrenoy & Silveira (2011)	Re-analysis of subset of data from Shay et al. (2005) N=114	14 weeks of: Acupuncture Placebo (control acupuncture points)	Mean pain score (Dorothy scale) Global rating of pain relief Attrition Mortality (over 2 years)	6 weeks 18 weeks	Reduced attrition in acupuncture group Lower mortality in acupuncture group	3
Phillips et al. (2004)	Case series N=21	10 sessions of acupuncture over 2 weeks	Pain Rating Scale Subjective Peripheral Neuropathy Screen (SPNS)	3 weeks	Reduced pain (present pain, best pain, worst pain, and total pain summary scores) Less symptoms (pain/itching/burning; pins and needles; numbness; total summary scores) in SPNS	4

**Bottom Line:** Re-analysis of data from one RCT found lower pain intensity in acupuncture compared to placebo. (Note: In the U.S., acupuncture is not practiced by PTs unless they have concurrent certification as an acupuncturist.)

1. Kietrys, D.M., Galantino, M.L., Beithoff, C., Benavente, E., Carey, W., Grove, L., & Norman, G. Physical therapy interventions for HIV-related distal sensory polyneuropathy: A systematic review. Poster presented at 4<sup>th</sup> International Workshop on HIV and Aging, Baltimore MD, Nov. 2013.

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Physical Therapy and Acupuncture for HIV Associated Distal Sensory Polyneuropathy (DSP): A Systematic Review<sup>1</sup>

Summary of Physical Therapy Studies

Citation	Study Design	Intervention(s)	Outcomes	Times(s) to Outcomes	Key Findings	Citation
McKeay et al. (1993)	Retrospective case series	Mean of 4.7 visits including: Microcurrent, Massage, Joint mobilization	Pain, Gait	n/a	"Pain absent or reduced" in 97% "Gait improvement" in 76%	4
Galantino et al. (1999)	Pilot study (repeated measures)	30 daily sessions of electroacupuncture (low voltage)	MOS-HIV (quality of life), Total II reflex parameters	4 weeks	Reduction in pain in 5 or 7 patients Improved functional activity (MOS-HIV) Improved firmness, M response and M response latency	4
Gale (2001)	Case study	5 visits over: 2 months (patient 1) 5 weeks (patient 2) Joint mobilization Gait tissue mobilization Stretching exercises Microcurrent Home program (stretching and desensitization)	Subjective pain and symptoms reports Gait analysis Muscle strength	After session After 5 sessions 6 months 1 year 18 months	Patient 1: decreased atrophy (after 1 visit), resolution of numbness (6 mo.), decreased pain (from 3 visits forward), improved gait (from 6 mo forward) Patient 2: improved sensation (6 mo.), decreased pain (from 1 visit forward), return to work (6 mo)	4

**Bottom Line:** Low level evidence suggests PT may help improve pain, gait, function, and sensation, but rigorous RCTs are needed to confirm such findings.

1 Kietrys, D.M., Galantino, M.L., Balthoff, C., Reschner, E., Carey, W., Green, L., & Homan, G. Physical therapy interventions for HIV-related distal sensory polyneuropathy: A systematic review. Poster presented at 4<sup>th</sup> International Workshop on HIV and Aging, Baltimore MD, Nov. 2013.

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Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

**Purposes**

- Compare QOL and self-reported lower limb function in HIV+ patients with and without DSP
- Determine the degree to which self-reported lower limb function predicts QOL
- Evaluate agreement (concordant validity) between the Lower Extremity Function Scale (LEFS) and the Lower Limb Functional Index (LLFI) in this population
- Describe utilization of health care resources for pain management in HIV+ patients with and without DSP.

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Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

**Methods**

- Participants were patients at an infectious disease practice in southern NJ / summer 2012
- Inclusion criteria: history of HIV disease, ambulatory, ability to read and write in English.
- Exclusion criteria included active opportunistic infections or uncontrolled psychiatric disorders
- Data collection:
  - Demographic questionnaire and chart review
  - MOS-HIV (Physical Summary Score and Mental Summary Score)
  - LEFS
  - LLLFI

*LEFS and the LLLFI data was expressed as a percentage with the same range and direction (0%=maximally impaired function; 100%=full function).*

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Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

**Mean LLFI and LEFS Values by Foot DSP Diagnosis (n=82)**

	Participants without Foot DSP				Participants with Foot DSP				p <sup>1</sup>
	N	Mean (min-max)	SD	Median	N	Mean (min-max)	SD	Median	
LLFI	28	76.2 (30-100)	27.1	93	54	43.4 (0-100)	24.1	42	<0.001
LEFS <sup>2</sup>	27	62.2 (17.5-100)	22.4	76	53	40.9 (2.5-100)	19.7	39	<0.001

<sup>1</sup> Mann-Whitney test, significance tests are within tools  
<sup>2</sup> n=80, data missing on 2 participants

**Bottom Line:** Self-reported LE function significantly lower in HIV+ patients with DSP than without DSP.

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Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

**Physical and Mental Quality of Life Scores by Foot Neuropathy Diagnosis (n=74)**

	Participants without foot DSP			Participants with foot DSP			p <sup>1</sup>
	N	Mean	SD	N	Mean	SD	
Physical Summary Score <sup>2</sup>	24	47.9	23.2	50	32.7	19.2	<0.001
Mental Summary Score <sup>2</sup>	24	47.8	28.0	50	38.3	23.2	0.134

<sup>1</sup> General linear model, adjusted for sex, age, years with HIV, HIV disability and interactions significance tests are within summary scores. Note: 8 of the 82 participants with complete MOS-HIV data were missing data regarding years with HIV or years receiving disability, thus n=74 are included in this analysis.  
<sup>2</sup> Normalized

**Bottom Line:** Physical Summary Score component of quality of life (MOS-HIV) significantly lower in HIV+ participants with DSP than those without.

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Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

- Relationship between QOL, potential confounders, and LE function
- Regression models of the effects of LLLFI and LEFS predicting physical and mental quality of life were statistically adjusted by including potential confounders (employment status, disability benefit status, presence of foot DSP, age, and PT treatment); this resulted in parameter estimates of the relationships of LEFS and LLLFI and the quality of life variables after controlling for the effects of the covariates.
- **BOTTOM LINE:** Lower limb function scores were highly predictive of both physical and mental QOL after controlling for confounders.
  - The models predicted between 68% and 75% of the variance in physical quality of life and approximately 31% of the variance in mental quality of life (physical quality of life: R<sup>2</sup>=.675 for LLLFI and R<sup>2</sup>=.749 for LEFS; mental quality of life: R<sup>2</sup>=.310 for LLLFI and R<sup>2</sup>=.309 for LEFS (p<.001 for all models)
- Of potential confounders entered into the models, only employment status was associated with physical summary score aspect of QOL (after controlling for LLLFI and LEFS scores).

**RUTGERS** Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

Bland-Altman analysis to assess agreement between LEFS and LLFI. (+) score indicates LEFS overestimates LLFI (i.e., LLFI indicates that the patient has a lower level of functioning than LEFS), and a (-) score indicates that LEFS underestimates (i.e., patient has lower function) than LLFI.

Band of clinically relevant agreement: 11.25 points (MCID of the LEFS)

Mean difference in LEFS and LLFI was 6.2 (significantly different than zero) indicating that, on average, LEFS overestimates LLFI by about 6 points

LEFS approximates LLFI within the band of clinical agreement in 58.8% (n=47) of the subjects, underestimating LLFI (indicating worse function) in only 10% of the cases (n=8), while overestimating LLFI in 31.3% (n=25) of the subjects.

LLFI is likely to classify patients as having a level of physical functioning equal to or lower than LEFS in 90% of subjects. LLFI is more likely to identify patients as having lower self-reported function than the LEFS.

A similar pattern was found when LEFS and LLFI were further analyzed subgrouping for patients with and without DSP. The LLFI was even more likely to indicate impairments in lower extremity function in HIV patients with DSP than the LEFS.

**RUTGERS** Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

Analysis of the magnitude of disagreement between LEFS and LLFI revealed a wider degree of disagreement among patients with DSP than in patients without DSP with an interquartile range (IQR) among patients with DSP (IQR=19.3) approximately 3.7 times greater than the IQR for patients without DSP (IQR=5.3)

This indicates that not only can the clinician expect LEFS to overestimate LLFI, but the degree of overestimate is likely to be even less predictable in patients with DSP than in patients without DSP.

**Bottom Line:** Our findings suggest the the LLFI may be preferable to the LEFS to identify activity limitations (functional impairments) in patients with HIV-related DSP.

**RUTGERS** Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

Pain Treatment Differences of Participants with and without DSP (n=82)

	Participants without DSP		Participants with DSP		Total	p <sup>1</sup>
	N	%	n	%	N	%
<b>Medical Treatment</b>						
No	24	88.9	11	20.0	35	42.7
Yes	3	11.1	44	80.0	47	57.3
<b>Physical Therapy Treatment</b>						
No	27	100.0	39	70.9	66	80.5
Yes	0	0.0	16	29.1	16	19.5
<b>CAM Treatment</b>						
No	26	96.3	29	52.7	55	67.1
Yes	1	3.7	26	47.3	27	32.9
Total	27	100.0	55	100.0	82	100.0

<sup>1</sup> Chi square test of independence

**Bottom Line:** Significant higher rates of utilization of pain management (medical or PT or CAM) in HIV+ participants with DSP.

**RUTGERS** Quality of Life and Self-Reported Lower Extremity Function in Adults with HIV-related Distal Sensory Polyneuropathy (Galantino, Kietrys, et al., submitted)

- Limitations
  - Sample of convenience may explain our observed DSP prevalence rate (67%)
  - Dx of DSP based on self-report (with confirmation from medical chart when possible)
  - Due to our small size, post hoc analysis revealed we were underpowered to detect a difference in Mental Health Summary Scores.
  - Reliance on self-report of function / activity limitation
  - We did not determine prevalence of diabetes or diabetes-related DSP in our sample

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**Our next study (spring/summer 2014) . . .**

**The Effects of Yoga on Persons with HIV-related Distal Sensory Polyneuropathy**  
Kietrys, Galantino et al, funded by Oncology Section of APTA

Repeated measures single group pilot study to determine feasibility and effect sizes

Intervention: 4 weeks of twice weekly yoga class and home practice

Proposed Outcomes

- Quality of Life (MOS-HIV)
- Pain
- Self-reported perception of neuropathy symptoms
- LE Function (LLFI and 5 time sit to stand test)
- Temporal and Spatial Gait Characteristics (GAITrite data, 6 min walk test)
- Vibration sense (biothesiometry)

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*Thank You*

**Questions**