Correlates of Self-Rated Health in Patients with Diabetic Peripheral Neuropathy: A Longitudinal Study

Running title: Diabetic Peripheral Neuropathy and Self-Rated Health

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Bulleted novelty statement:

- Self-rated health (SRH) is a robust independent predictor of morbidity and mortality in various populations, including persons with diabetes. However, the correlates of SRH among people with complications of diabetes remain understudied.
- Objectively assessed diabetic peripheral neuropathy (DPN) severity was associated with lower SRH, and this relationship appeared to be mediated by associated increases in DPN-related symptoms, DPN-specific limitations in daily activities, and depression symptoms.
- The finding that SRH is linked to important health indicators among those with DPN support the growing interest to systematically assess SRH and other patient-reported outcomes in diabetes research and care.

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Abstract

OBJECTIVE: Self-rated health (SRH) is a robust predictor of morbidity and mortality in various populations, including persons with diabetes. The aim of this longitudinal investigation was to examine correlates of SRH in adults with diabetic peripheral neuropathy (DPN).

RESEARCH DESIGN AND METHODS: Participants (n=295; age M(SD)=61.5±10.7 years; 70% male; 73% type 2 diabetes) provided SRH (SF-12) at baseline and 18-months, and completed the Neuropathy and Foot Ulcer-Specific Quality of Life measure assessing DPN-symptoms of pain, unsteadiness and reduced sensation in feet, DPN-specific limitations in daily activities, and DPN-specific distress. The Hospital Anxiety and Depression Scale assessed symptoms of depression. DPN severity was assessed with the Neuropathy Disability Score and the Vibration Perception Threshold.

RESULTS: At baseline, greater neuropathy severity was associated with worse SRH when controlling for covariates (coef.[95%CI]=-.06[-.11-.01]). This relationship appeared to be mediated by symptoms of reduced feeling (-.11[-.20-.01]), increased pain (-.17[-.31-.02]) and increased unsteadiness (-.16[-.28-.04]), greater limitations in daily activities (-.13[-.22-.04]) and more depression symptoms (-.09[-.12-.05]). SRH was reasonably stable over 18 months when adjusting for predictors (*ICC*=0.59[0.51-0.67]). At 18-months, unsteadiness (-.07[-.19-.01]), limitations in daily activities (-.08[-.14-.02]), depression symptoms (-.06[-.09-.04]) and distress (-.10[-.20-.001]) showed independent associations with worse SRH.

CONCLUSIONS: Results identify independent correlates of SRH among adults with diabetic peripheral neuropathy and suggest that, if these effects represent causal relationships, neuropathy severity affects patients' perceptions of their health through the experience of DPN-related symptoms, limitations in daily activities, and depression symptoms and DPN-related emotional distress.

Keywords: diabetic peripheral neuropathy, self-rated health, unsteadiness, depression symptoms, diabetes-related distress.

Patient-reported outcomes (PROs) are increasingly important in clinical practice and clinical trials to capture valuable information about health status and burdens of treatment, not otherwise reflected in objective or biological measures. One central PRO is self-rated health (SRH), which refers to a person's perceptions of their general health and incorporates social, psychological and biological aspects of the self (1). Despite robust controls for potential confounding variables, responses to various single-item measures of SRH consistently and robustly predict morbidity and mortality (2), including among individuals with diabetes (3). SRH has been shown to predict diabetic foot ulcerations (DFUs) and amputations over 2.4 years of follow-up among individuals with type 2 diabetes after adjustment for established risk factors and clinical history (4). While complications of diabetes such as diabetic peripheral neuropathy (DPN) show a consistent relationship with poorer SRH (e.g., 5), the correlates of SRH among people with complications of diabetes remain understudied.

Diabetic peripheral neuropathy is the most prevalent complication of diabetes, affecting up to 50% of individuals with diabetes (6) and leading to severe morbidity and extremely high health care costs (7). Patients experience impaired quality of life (QOL) due to neuropathic pain, loss of sensation leading to poor balance, falls, foot deformities, and high rates of ulceration and amputation (8). DPN is a source of significant emotional distress, with DPN symptoms and associated limitations in functioning accounting for nearly half of the variance in depression symptom scores (9,10). DPN-related unsteadiness is one of the strongest predictors of depression symptoms in this patient population (9,10) and could be an important influence on non-adherence to offloading interventions (11). An earlier cross-sectional study linked DPN symptoms of numbness and loss of sensation with lower overall SRH (5), but the whole range of DPN symptoms was not evaluated and clinical indicators of DPN severity were not available.

The current study explores independent correlates of patients' perceptions SRH over time among individuals with DPN. We hypothesized that increased DPN severity would be associated with lower SRH, independent of demographic and other disease-related characteristics. We also hypothesized that DPN severity would be associated with SRH through the experience of DPN-related symptoms and limitations in daily activities. Finally, we expected that factors would show consistent associations with SRH over time. A better understanding of correlates of SRH in patients with DPN may shed light on the factors that could influence perceptions of health among these patients and would provide evidence for the validity and clinical significance of SRH as a PRO among individuals with DPN.

RESEARCH DESIGN AND METHODS

Participants and Procedures

A total of 295 individuals with Type 1 or Type 2 diabetes and moderate-to-severe DPN who provided SRH at baseline and 18-months were included in the current analyses. These individuals were recruited from specialist diabetes centers in the UK (Manchester) and USA (Baltimore, MD and State College, PA) for participation in an 18-month study examining the psychological determinants of foot self-care adherence and foot ulceration; further details of this sample have been previously described (9,10,12). Two tests were used to establish the presence of DPN in accordance with diagnostic guidelines (6): the neuropathy disability score (NDS) and the vibration perception threshold (VPT), which are further described in the 'Measures' section. Patients were included if VPT $\geq$ 25 volts and NDS $\geq$ 3. Those with milder DPN severity and those who had significant peripheral vascular disease (< 1 palpable pulse per foot and/or history of bypass surgery), history of major amputation (> a single digit), advanced diabetes

complications (e.g., end-stage renal disease), other severe medical conditions (e.g., stroke), or insufficient English comprehension were excluded from participation.

The study was approved by the Central Manchester Research Ethical Review Committee and the Institutional Review Boards at the Johns Hopkins University and the Pennsylvania State University, and informed consent was obtained from all participants.

Measures

Demographic, disease and trait characteristics. Demographic and clinical characteristics assessed included age, sex, education, marital status, type and duration of diabetes, diabetes complications (retinopathy, nephropathy, and cardiovascular disease), and number of comorbid illnesses. Neuroticism was included to adjust for a general predisposition to experience negative affect and was measured by the Big Five Inventory (8 items) (13), which showed good internal consistency in this sample (alpha=.82). Presence of retinopathy and nephropathy, and age were reassessed at 18-months.

DPN Severity. The VPT was assessed at the great toe in both feet in triplicate, using a neurothesiometer (Horwell, Nottingham, UK). The NDS score was derived from examination of pain, vibration, temperature sensation and Achilles reflex. A score of 0 represents a normal nervous system examination and the maximum score was 10 (14). NDS was reassessed at 18 months.

DPN-related Symptoms and Functioning. The NeuroQol, a measure of quality of life developed specifically for individuals with DPN (15), includes neuropathic symptoms of reduced feeling (3 items), pain (7 items), and unsteadiness (3 items), DPN-related limitations in daily activities (3 items), and DPN-specific distress (11 items). Higher scores indicate greater endorsement of symptoms and limitations in functioning. Internal consistency for DPN

symptoms, DPN-related limitations in daily activities, and DPN-specific distress was good to excellent (alphas = .86-.90). The NeuroQol was administered at both baseline and 18 months.

History of DFUs. Individuals were coded as having a positive history of DFU if they self-reported a prior DFU or had an active DFU determined by a medical examination. A history of DFUs was obtained by asking each subject: "Have you ever had a foot ulcer (an open sore on your foot)?" Those answering in the affirmative were verified by examination of medical records and careful podiatric assessment. A foot ulcer was defined as a full thickness skin break below the malleoli. A history of DFUs was assessed only at baseline.

Emotional Distress. Assessment of DPN-specific distress using the NeuroQol is described above. Depressive symptoms were assessed using the 7-item Hospital Anxiety and Depression Scale (HADS) (16). The HADS was selected as it was designed to reduce confounding of somatic symptoms that commonly occur in the presence of physical illness. Questions included both positive *(e.g., I can laugh and see the funny side of things)* and negative (*e.g., I feel as I am slowed down)* endorsement of depression. Questions were coded so that higher scores indicate greater severity of symptoms. Internal consistency was good (alpha = .84). Emotional distress measures were administered at both time points.

Self-Rated Health. SRH was measured by a single item from the SF-12 (17) at baseline and the 18-month follow-up, *"In general, would you say your health is excellent, very good, good, fair, or poor?"* Responses were rated on a 1-5 scale and were reverse coded so that higher scores indicate better health.

Statistical Analyses

Descriptive statistics were assessed for all study-related variables. Bivariate associations were examined using Pearson's r for continuous study variables, and t-tests or chi square for categorical study variables.

Six regression models were run to explore the association between hypothesized correlates and SRH assessed at baseline, as follows: 1) control variables (demographic/ disease/ personality characteristics), 2) objective indicators of neuropathy severity (NDS and VPT scores), 3) History of DFUs, 4) DPN-related symptoms, 5) DPN–related limitations in daily activities, and 6) depressive symptoms and DPN-specific distress. These variables were entered in separate steps to test independent associations with SRH in a way that aligned with our hypotheses.

One mixed-effects regression model was run (model 7), with random intercepts at the patient level, to test whether factors were consistently associated with SRH over time. This model was selected as SRH remained relatively stable over time; and it tests the relationship between correlates and SRH at 18-months while accounting for multiple assessments. This model only included variables collected at both baseline and 18-months.

Data were considered to be missing at random, with no demographic or illness differences between those missing and not missing data. There were 9 variables with some missing values, ranged from 1 missing value for the presence of CVD to 9 for the presence of retinopathy. We ran multiple imputation analyses for baseline models to account for missing data. Parameters were estimated within each dataset individually and then combined using Rubin's rules (18). Analyses were conducted using Stata 15.1 (19).

RESULTS

Sample Characteristics

Descriptive characteristics of the study sample are presented in **Table 1**. The majority of participants were White, male, older adults diagnosed with Type 2 diabetes. In this population with DPN, retinopathy (44.1%) and cardiovascular disease (34.9%) were the most common additional diabetes complications reported. At baseline, 38.3% of subjects either reported a previous or active DFU. The most commonly endorsed SRH score indicated "Good" health (37.6%), followed by "Fair" health (31.2%). The mean HADS score (4.93 ± 3.81) was within the "normal" range (21), and the mean DPN-emotional distress score (2.3 ± 1.2) indicated average distress (20).

Site comparisons (UK vs US) indicated that US participants reported more comorbid disorders, more DFUs, higher VPT scores indicative of more severe DPN, and lower self-reported functioning as assessed by the NeuroQoL.

Summary of Findings

Baseline Analyses

Results of the six stepped regression models are shown in **Table 2**. Model 1 examined demographic and disease correlates of baseline SRH; being in the US (p=.022), younger age (p=.003), presence of CVD (p=.001), higher number of comorbidities (p=.027) and neuroticism (p<.001) showed independent associations with lower baseline SRH. When NDS and VPT scores were added to the model (Model 2), NDS scores independently predicted baseline SRH (p=.033). The addition of DFU history to create Model 3, did not support an independent association with baseline SRH. When DPN symptoms assessed by the NeuroQOL were added to create Model 4, reduced feeling (p=.032), pain (p=.031) and unsteadiness (p=.010) showed independent associations with baseline SRH and attenuated the effect of NDS on baseline SRH. When DPN-specific limitations in daily activities scores from the NeuroQol were added to

model 5 (**Table 2**) this also showed an independent association with baseline SRH (p<.01) and attenuated the independent associations between reduced feeling and pain symptoms with baseline SRH, with only symptoms of unsteadiness continuing to show an independent association with SRH (*p*=.040). Finally, when depression and DPN-specific distress were included in model 6, depression symptoms showed an association with baseline SRH (p<.001) and attenuated the effect of DPN-specific limitations in daily activities and unsteadiness (**Table 2**, Model 6). In this final model, being in the US (*p*=.045), younger age (*p*=.011), presence of CVD (*p*=.003), a higher number of comorbidities (*p*=.049), neuroticism (*p*=.049), a lower VPT score (*p*=.026), and depression symptoms (p<.01) indicated an independent association with lower SRH.

Longitudinal Analyses

The intra-class correlation between SRH at baseline and 18 months was 0.59 (95%CI: 0.51-0.67) when accounting for the predictors in the model, suggesting a reasonably good stability of SRH over time. The mixed-effects model indicated that being in the US (*p*=.017), reporting more unsteadiness (*p*=.029), a higher level of DPN-specific limitations in daily activities (*p*=.015), higher levels of depression symptoms (*p*<.01), and DPN-specific distress (*p*=.048) were each independently related to higher SRH at 18-months when accounting for multiple assessments (**Table 3,** Model 7).

DISCUSSION

The goal of this study was to identify correlates of patients' perceptions of their health, and assess these associations longitudinally, among a sample of patients with DPN. Our findings extend work of Klein and colleagues (5) conducted over 30 years ago that demonstrated self-reported neuropathy symptoms were strongly associated with lower SRH among 937 diabetes

patients. Our work reproduces these findings using objective measures of DPN. This is important because self-reported symptoms of DPN do not consistently correlate with objective measures of DPN severity (20), and because self-reported and objectively measured DPN symptoms can differ in their relationship to patient outcomes (9). If these effects represent causal relationships, results further suggest that neuropathy severity affects patients' perceptions of their health through the experience of DPN-related symptoms, limitations in daily activities, and depression symptoms and DPN-related emotional distress. Results also supported that SRH was reasonably stable over an 18-month period, which may reflect the fact that examined correlates (and complications like DPN) are likely to be relatively stable over an 18-month time frame. While not all measures were assessed at both time points, greater DPN-related unsteadiness, greater DPN-specific limitations in daily activities, and higher depression symptoms consistently showed independent associations with SRH over time.

This study also identified several demographic and disease-related characteristics as independent correlates of lower SRH among persons with DPN. This included living in the US, younger age, presence of CVD, a higher number of comorbidities, and neuroticism. The independent association between living in the US compared to the UK and lower SRH scores, in addition to observed group differences (e.g., higher disease severity and lower functioning among individuals from the US), may reflect cultural differences, or differences in recruitment or access to social services and health care between countries. The independent association observed between younger age and lower SRH may be reflective of an earlier onset of DPN, though previous literature on the relationships between age, age of illness onset, and SRH show mixed findings that may differ by gender (3,5). Future work should continue to examine how these factors relate to SRH and health outcomes over time among individuals with DPN.

A history of DFUs was not independently associated with patients' perceptions of health when adjusting for demographic factors, comorbid health conditions, and severity of DPN. This adds to findings of a population-based study conducted in Norway that reported an independent relationship between SRH and DFU history when adjusting for demographic factors, comorbid health conditions, lifestyle variables, and illness-related variables such as insulin use, A1C, and diabetes duration (21). This Norwegian study differed from the current study in that they assessed a population-based sample of individuals with diabetes, rather than a sample of individuals diagnosed with DPN. Relatedly, while Iversen and colleagues (21) accounted for variables related to disease severity, they did not control for severity of neuropathy. Additionally, a history of DFUs were assessed only via self-report in the Norwegian study, while the current study verified self-reports by examination of medical records and podiatric assessment. Additional research is needed to reach a clearer answer on the independent association of DFU history and SRH among various diabetes samples.

While we are not able to establish causality, our work shows that physical symptoms, DPN-specific limitations in daily activities and depressive symptoms may be a mechanism by which DPN severity contributes to reduced SRH. This is consistent with previous data showing that physical symptoms and functional status predict SRH among individuals with type 2 diabetes (22). Heightened emotional distress has been posited as a pathway through which DPN symptoms like unsteadiness negatively impact SRH and QOL (23), and previous data from this cohort showed that DPN-specific symptoms and limitations in daily activities were predictive of depression symptom severity cross-sectionally and over time (9,10). The current findings are consistent with a pathway of DPN-severity contributing to SRH ratings through increased symptoms, reduced functioning, and increased emotional distress.

Previous research suggests that both physical and emotional functioning contribute to SRH. Our finding that depressive symptoms showed the largest predictive power among persons with DPN maps onto an inconsistent literature. Previous research supports that physical symptoms and other health-related measures show the largest predictive power compared to psychological well-being in a population-based study (1) and among individuals with diabetes (24). Yet, other population-based studies show depression to be one of the largest predictors of fair or poor SRH (e.g., 25). It is possible that the relative strengths of relationships between emotional and physical functioning and SRH may differ among different samples or with the inclusion of different measures of physical and emotional functioning.

The current study is limited in that it consists of two discrete (US and UK) samples of mostly White men, which limit generalizability of findings. Further, causal inferences cannot be made from this study: future studies with an experimental design that may manipulate correlates of SRH (e.g., one's level of unsteadiness, emotional distress) would allow for better assessment of the direction of influence underlying the observed associations between patient and illness factors and SRH over time.

It is difficult to make specific clinical recommendations until DPN-related correlates of SRH are further clarified. It may be beneficial for clinicians to be more attentive to DPN symptom severity and particularly unsteadiness, as this symptom is often under-reported and underdiagnosed (20). Recent work has shown that perceived DPN-related unsteadiness is closely associated with gait laboratory assessments of walking and balance impairment, thus individuals with DPN appear to have a good sense of their level of impairment (26). It may be beneficial to assess the impact of experienced symptoms on limitations in daily activities and emotional well-being. Once identified, multifaceted interventions that target both biomechanical difficulties and

emotional distress among patients with DPN hold the potential to improve SRH as well as QOL (27). Future research should test such integrative interventions and continue to model the myriad of aspects of health, well-being an expectations that come together to contribute to the important PRO of SRH among individuals with DPN.

Inclusion of PROs such as SRH in DPN-related clinical care and research promotes a patient-centered focus, and SRH may be particularly useful in that it consists of a single-item question that can be easily incorporated into health services and research. Future research should examine whether perceptions of health predict important medical outcomes such as mortality in this patient population. This would contribute to our understanding of SRH as a risk factor for negative health outcomes as diabetes progresses and patients develop complications. Additionally, further work is needed to better understand how SRH maps onto other important PROs such as QOL, and the importance of distinguishing health status from QOL has been reviewed (e.g., 28,29). The finding that SRH is linked to multiple important health indicators support the growing interest to systematically assess PROs as primary outcomes in diabetes research. Importantly, centering PROs like SRH in diabetes research and care aligns with American Diabetes Association's recommendations for a patient-centered approach to diabetes care (30).

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Characteristics	UK (n=179)	USA (n=116)	Total (n=295)
Female Gender	29.1%	32.8%	30.5%
Age	61.2 ± 11.3	61.9 ± 9.7	61.5 ± 10.7
Education:			
Primary	4.0%	0.9%	2.8%
Secondary	54.3%	42.5%	49.7%
Some College	28.0%	14.2%	22.6%
College Grad	7.4%	26.5%	14.9%
Postgraduate	6.3%	15.9%	10.1%
Marital Status (living alone)	31.8%	25.0%	29.2%
Diabetes Type (type 2)	65.9%	82.8%	72.7%
Retinopathy	45.0%	42.6%	44.1%
Nephropathy	14.0%	16.4%	14.9%
Cardiovascular Disease	31.3%	40.5%	34.9%
Concomitant Disorders (#)	0.7 ± 0.9	1.5 ± 1.3	1.0 ± 1.1
DPN Severity:			
Neuropathy Disability Score	7.3 ± 2.3	7.5 ± 2.2	7.4 ± 2.3
Vibration Perception Threshold	39.3 ± 9.5	45.4 ± 8.4	41.8 ± 9.5
Foot Ulcer:			
Ever/Current	30.2%	50.9%	38.3%
Neuroticism	2.7 ± 0.7	2.7 ± 0.6	2.7 ± 0.7
NeuroQoL – Pain	1.9 ± 0.8	1.9 ± 0.7	1.9 ± 0.8
NeuroQoL – Reduced Feeling	2.6 ± 1.5	3.5 ± 1.3	2.9 ± 1.5
NeuroQoL – Unsteadiness	2.1 ± 1.2	2.4 ± 1.1	2.2 ± 1.1
NeuroQoL – Limitations daily activities	2.3 ± 1.3	2.9 ± 1.3	2.5 ± 1.4
HADS Depression	5.1 ± 4.1	4.7 ± 3.4	4.9 ± 3.8
Self-Rated Health	3.3 ± 1.1	3.2 ± 0.9	3.2 ± 1.0

Note: Values are percentages and means ± standard deviations.

Table 1. *Sample Characteristics*

Variables	Model 1 Coef.(95%CI)	Model 2 Coef.(95%CI)	Model 3 Coef.(95%CI)	Model 4 Coef.(95%CI)	Model 5 Coef.(95%CI)	Model 6 Coef. (95%CI)
Demo/Disease/Trait						
Country	.27(.04-.50)	.24(.01-.48)	.25(.01-.49)	.31(.08-.54)	.34(.11-.57)	.23(.01-.46)
Female Sex	-.09(-.32-.15)	-.08(-.32-.15)	-.08(-.32-.16)	-.01(-.24-.22)	.004(-.22-.23)	.02(-.19-.24)
Type 2 Diabetes	-.28(-.56-.01)	-.30(-.58--.02)	-.30(-.58--.02)	-.20(-.47-.07)	-.20(-.46-.07)	-.17(-.42-.09)
Age	.02(.01-.03)	.02(.01-.03)	.02(.01-.03)	.02(.004-.03)	.01(.003-.03)	.01(.003-.03)
Retinopathy	-.18(-.41-.05)	-.15(-.38-.08)	-.14(-.38-.09)	-.10(-.32-.12)	-.10(-.32-.12)	-.09(-.30-.11)
Nephropathy						
Some	-.29(-.59-.01)	-.28(-.58-.02)	-.27(-.58-.03)	-.23(-.51-.06)	-.20(-.49-.08)	-.18(-.45-.09)
Dialysis	-.38(-1.4-.68)	-.31(-1.4-.75)	-.30(-1.4-.75)	-.34(-1.3-.66)	-.31(-1.3-.68)	-.38(-1.3-.57)
CV Disease	-.38(-.61--.15)	-.39(-.62--.17)	-.39(-.62--.17)	-.33(-.55--.12)	-.31(-.53--.10)	-.31(-.52--.11)
Comorbidities	-.12(-.22--.01)	-.11(-.22--.01)	-.11(-.22--.01)	-.08(-.18-.02)	-.09(-.19--.01)	-.09(-.19--.001)
Neuroticism	-.49(-.65--.32)	-.49(-.65--.33)	-.49(-.65--.33)	-.34(-.51--.18)	-.32(-.48--.15)	-.17(-.34--.001)
DPN Severity						
NDS		-.06(-.11--.01)	-.06(-.11--.01)	-.01(-.05-.06)	.002(-.05-.06)	-.01(-.04-.06)
VPT		.01(-.01-.02)	.01(-.01-.02)	.01(-.002-.02)	.01(-.001-.02)	.01(.002-.03)
DFU History			-.05(-.29-.20)	-.03(-.26-.21)	.04(-.20-.27)	.002(-.23-.24)
DPN Symptoms						
Reduced Feeling				-.11(-.20-.01)	-.08(-.18-.02)	-.06(-.15-.04)
Pain				-.17(-.31-.02)	-.13(-.28-.03)	-.01(-.17-.14)
Unsteadiness				-.16(-.28-.04)	-.13(-.25-.01)	-.07(-.19-.05)
DPN-specific Limitations in Daily Activities					-.13(-.22-.04)	-.09(-.18-.01)
Emotional Distress						
Depressive Sx						-.09(-.12-.05)
DPN-specific distress						-.03(-.17-.12)
Joint Significance Test	3.5(2.6-4.3)	3.6(2.7-4.6)	3.6(2.7-4.6)	3.6(2.6-4.5)	3.6(2.7-4.6)	3.1(2.2-4.0)

Table 2. *Regression Models Predicting SRH at Baseline*

Variables	Model 7 Coef.(95%CI)
Demo/Disease/Trait	
Time	-.06(-.15-.03)
Country	.22(.04-.41)
Female Sex	-.13(-.31-.06)
Type 2 Diabetes	-.18(-.40-.04)
Age	.01(-.00-.02)
Retinopathy	.02(-.16-.12)
Nephropathy	
Some	-.19(-.38-.01)
Dialysis	-.29(-.91-.33)
DPN Severity	
NDS	.02(-.01-.05)
DPN Symptoms	
Reduced Feeling	-.06(-.15-.04)
Pain	-.01(-.17-.14)
Unsteadiness	-.07(-.19-.-.01)
DPN-Specific Limitations in Daily Activities	-.08(-.14-.-.02)
Emotional Distress	
Depressive Sx	-.06(-.09-.-.04)
DPN-specific distress	-.10(-.20-.-.001)
Joint Significance Test	3.2 (2.6-3.9)

Table 3. *Mixed-effects Model Predicting SRH at 18 months*