Clinical Response to Real-Time Patient-Reported Diabetic Peripheral Neuropathy Symptoms

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ABSTRACT

Introduction: To assess clinician response to real-time patient-reported data about diabetic peripheral neuropathy (DPN) symptoms, we analyzed DPN diagnosis and treatment patterns after administration of a 4-question symptom questionnaire in a large vertically integrated health care system.

Methods: Retrospective cohort study to analyze data from 160,852 patients screened for DPN symptoms from April 2012 to March 2014. Electronic medical record data were used to study changes in DPN diagnosis, treatment initiation, and treatment intensification. We used logistic regression to study the association of patient characteristics with the odds of clinical response.

Results: Of patients queried, 50,684 (31.5%) reported symptoms. Patients reporting DPN symptoms experienced a greater increase in new DPN diagnoses (16 percentage points; $p < 0.0001$) and medication use (4 percentage points; $p < 0.0001$) compared with those denying symptoms. Among patients reporting symptoms, women and nonwhite patients were less likely to receive a DPN diagnosis, whereas older patients were more likely to receive a DPN diagnosis. Overall, patients who were older, were Asian (hazard ratio = 0.67, 95% confidence interval = 0.63-0.77), and had lower socioeconomic status (hazard ratio = 0.89, 95% confidence interval = 0.80-0.99) were less likely to be treated. However, these racial and socioeconomic differences were not statistically significant for patients with preexisting DPN diagnoses.

Conclusion: Patients' real-time reports of DPN symptoms were associated with increased clinical activity. Patient- and clinician-level factors associated with the likelihood of receiving a DPN diagnosis need further study because a formal diagnosis may be associated with more equitable treatment.

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is the most common complication of both type 1 and type 2 diabetes and affects about 50% of people with longstanding disease.[1] This condition costs the US an estimated $4 billion to $15 billion annually in health care costs and lost productivity. The negative impact of DPN on the health care system is likely to increase as the diabetes epidemic grows.[2] The devastating impact of DPN on the quality of life of individual patients with painful and uncomfortable symptoms (eg, pain, tingling, burning sensation, electric shock feeling) is well documented.[1]

Yet, DPN is often underrecognized and undertreated in primary care settings.[3,4] The gold standard for diagnosing DPN, according to the Toronto DPN Expert Group, should be nerve conduction studies; diagnosing DPN by signs and symptoms is not specific or sensitive enough for a definitive diagnosis.[5] However, this labor-intensive and expensive method is difficult to implement on a large scale. Thus, tools such as patient questionnaires about symptoms have been developed as less intensive methods of identifying patients with possible DPN or related conditions in real time during clinic visits.[6-12]

Little is known about how clinicians respond to the availability of these data in real time, particularly when they are employed on a systemwide scale. In 2012, a brief symptom questionnaire was integrated into the electronic medical record (EMR) in a large integrated health care system to identify uncontrolled symptoms associated with diabetes. This symptom questionnaire was implemented as part of a systemwide effort to improve screening for complications associated with longstanding diabetes to improve care for these complications.

The purpose of this study was to assess the impact of reporting DPN symptoms (eg, pain or paresthesias in the feet) on subsequent DPN diagnosis and treatment. We hypothesized that the integration into the EMR of patients' self-reported data on their DPN symptoms would be associated with an intensification of DPN recognition and management. Among those patients with symptoms, we further explored individual patient factors associated with the timing of new diagnoses, treatment initiation, and treatment titration.

METHODS

Study Design

A retrospective cohort study was conducted to assess implementation of the symptom questionnaire among 234,903 adult patients with diabetes within Kaiser Permanente Northern California (KPNC). KPNC is an integrated, prepaid multispecialty health care system consisting of a hospital system, physician group, and health insurance plan serving more than 4 million members. All clinical data were derived from the EMR of the KPNC medical system.

Study Population

The study population included patients who were diagnosed with diabetes and identified in the KPNC Diabetes Registry from April 2012 to March 2014 and who were older than age 18 years as of January 2, 2012. Although the type of diabetes is not available in the registry, we estimate that more than 95% of these patients have type 2 diabetes in accordance with national prevalence estimates.[13] According to data from

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the EMR in 2012 to 2014, we excluded patients who had any inpatient or outpatient diagnosis of substance abuse (International Classification of Diseases, Ninth Revision [ICD-9] codes 305.0, 305.2, 305.3, 305.4, 305.5, 305.6, 305.7, 305.8, 305.9, 291, 292, 303, or 304), gestational diabetes (ICD-9 code 648.8), dementia (ICD-9 codes 290.0, 290.1, 290.4, or 331.0), or hospice/palliative care (ICD-9 code V66.7) because these factors may have led to changes in care that were clinically appropriate but not necessarily consistent with guidelines. We further excluded patients who were not enrolled in the medical system for a full 12 months before and after their first screening from the pre-post analyses (described in "Statistical Analysis") and multivariate models to ensure adequate data capture.

Comparison Groups

The DPN symptom questionnaire was developed in response to a need to improve the diagnosis and treatment of DPN. It was available in the EMR at KPNC facilities in April 2012 after medical assistants were trained to use the questionnaire. Medical assistants were instructed to administer the symptom questionnaire to all patients with diabetes while measuring vital signs at the beginning of routine primary care visits. The patient reports were entered into the EMR for the physician to view, and a paper copy was handed to the physician before his/her patient contact. The questionnaire included 4 questions with simple yes or no answers inquiring about symmetrical foot pain and paresthesias to assess DPN symptoms, as well as calf pain, foot sores, and erectile dysfunction, which are also sequelae of poorly controlled diabetes. A questionnaire was flagged in the EMR if any of the questions was answered affirmatively. Previous studies of much longer, validated symptom questionnaires such as the Michigan Neuropathy Screening Instrument have shown high specificity for questions regarding foot pain and paresthesias (92.7%-98.2%), but low sensitivity for DPN (25%-37.6%).[12]

Because one of the primary outcomes of this study was to assess treatment response for neuropathic pain, we focused on the question assessing neuropathic pain symptoms by taking an affirmative response to the question about the presence of foot numbness, pain, and paresthesias as a "positive" screen. For the main analyses, described in "Statistical Analysis," we compared changes in health services use before and after the first observed DPN screen for patients who screened "positive" (presence of DPN symptoms) or "negative" (absence of DPN symptoms) for DPN symptoms.

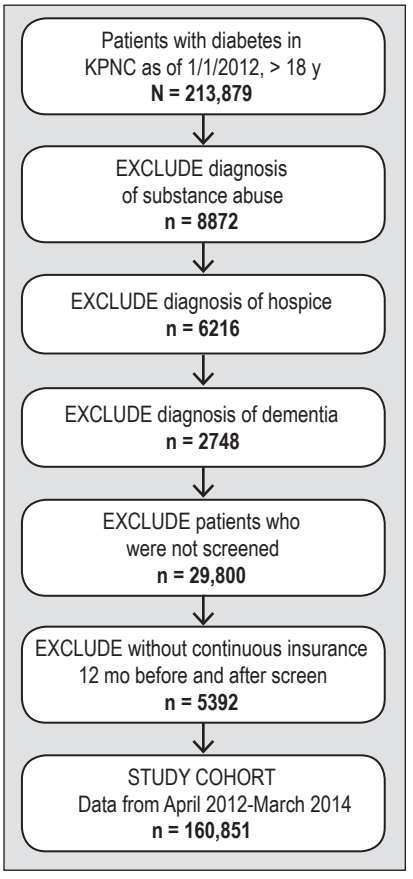

Figure 1. Study design with inclusion and exclusion criteria.
KPNC = Kaiser Permanente Northern California.

Outcome Measures

The primary outcomes for this study were 1) clinical documentation of DPN, defined as at least 1 inpatient or 2 outpatient diagnoses for peripheral neuropathy (ICD-9 codes 356.0, 356.9, or 357.2); 2) a new active prescription for at least 1 medication commonly used to treat DPN symptoms at the point of the screening visit or afterward (amitriptyline, nortriptyline, imipramine, desipramine, duloxetine, paroxetine, citalopram, pregabalin, venlafaxine, or gabapentin)[14]; and 3) intensification of

Nondiabetic Neuropathy Diagnoses[a]

265.x Thiamine and niacin deficiency states
266.0–266.9 Deficiency of B-complex components
277.1 Disorders of porphyrin metabolism
277.3 Amyloidosis
281.0 Pernicious anemia
281.1 Other vitamin B12 deficiency anemia
355.1 Meralgia paresthetica
355.5 Tarsal tunnel syndrome
356.4 Idiopathic progressive polyneuropathy
357 Inflammatory and toxic neuropathy
357.1 Polyneuropathy in collagen vascular disease
357.3 Polyneuropathy in malignant disease
357.4 Polyneuropathy in other diseases classified elsewhere
357.5 Alcoholic polyneuropathy
357.6 Polyneuropathy due to drugs
357.7 Polyneuropathy due to other toxic agents
357.8x Inflammatory and toxic neuropathy—Other
357.9 Inflammatory and toxic neuropathy—Unspecified
446.x Polyarteritis nodosa and allied conditions
714 Rheumatoid arthritis and other inflammatory polyarthropathies
723.0 Spinal stenosis in cervical region
724.00 Spinal stenosis in unspecified region
724.01 Spinal stenosis in thoracic region
724.02 Spinal stenosis, lumbar region, without neurogenic claudication
724.03 Spinal stenosis, lumbar region, with neurogenic claudication
724.09 Spinal stenosis of other region
724.3 Sciatica
443.9 Peripheral vascular disease unspecified
443.89 Other peripheral vascular disease
302.72 Psychogenic dysfunction with inhibited sexual excitement

[a] Diagnostic codes are from International Classification of Diseases, Ninth Revision.

therapy (minimum increase in the daily dose was 10 mg, except for pregabalin and gabapentin for which the minimum dose increase was 25 mg and 100 mg, respectively). For the pre-post analysis (described in "Statistical Analysis"), the DPN diagnosis and medication use were assessed during the 12 months before and after the first observed DPN screen. Treatment intensification was assessed during follow-up among those with evidence of prior DPN medication use.

Secondary outcomes relating to diabetes management included diagnoses for related pain conditions (a full list of corresponding ICD-9 codes is available in the Sidebar: Nondiabetic Neuropathy Diagnoses); tests; referrals to an endocrinologist, neurologist, and podiatrist; and the mean number of DPN medications prescribed. Baseline characteristics included age, sex, race (black, white, Hispanic, Native American/Alaskan Native, Pacific Islander/Native Hawaiian, Asian, multiracial), most recent hemoglobin A_{1C} (HbA_{1C}), previous opioid use, non-DPN neuropathy diagnoses, number of physician visits, and visits to the endocrinologist, podiatrist, and neurologist. We also categorized patients into quartiles of the neighborhood deprivation index, which is based on multiple domains of socioeconomic status derived from US Census tract data.[15]

Table 1. Baseline characteristics of analytic cohort (N = 160,851) stratified by screening status[a]

Characteristic	Screen: Do you have tingling, numbness, burning, or pain in your feet?[b]	
	Yes, no. (%): 50,684 (31.5)	No, no. (%): 110,167 (68.5)
Age as of January 1, 2012, mean (SD), y	64.0 (12.0)	61.8 (13.3)
Opioid use in last 90 days	10,426 (42.0)	14,383 (58.0)
Sex		
Women	25,929 (33.3)	51,890 (66.7)
Men	24,755 (29.8)	58,277 (70.2)
Race/ethnicity[c]		
American Indian/Alaska Native	360 (34.5)	684 (65.5)
Asian	8129 (24.0)	25,735 (76.0)
Black	5090 (31.8)	10,934 (68.2)
Hispanic	8276 (29.8)	19,478 (70.2)
Native Hawaiian/Pacific Islander	422 (28.2)	1076 (71.8)
White	25,557 (35.5)	46,444 (64.5)
Multiple race	2358 (34.8)	4414 (65.2)
Most recent HbA_{1C} before screen		
< 7% (53 mmol/mol)	18,900 (30.1)	43,948 (69.9)
7%-9% (53-75 mmol/mol)	21,473 (32.2)	45,176 (67.8)
> 9% (75 mmol/mol)	7060 (35.4)	12,870 (64.6)
Neighborhood deprivation index[c]		
First quartile: Least deprived	10,151 (29.7)	24,010 (70.3)
Second quartile	14,141 (31.2)	31,195 (68.8)
Third quartile	14,777 (32.0)	31,377 (68.0)
Fourth quartile: Most deprived	10,880 (33.0)	22,065 (67.0)
Related complications[c]		
Do you have skin sores or open wounds on your feet?		
Yes	5194 (63.2)	3024 (36.8)
No	45,242 (29.8)	106,855 (70.3)
Do you get pain in your calves when you walk?		
Yes	17,783 (60.2)	11,736 (39.8)
No	32,521 (25.0)	97,723 (75.0)
Have you ever had problems with erections due to your diabetes?		
Yes	10,122 (42.5)	13,715 (57.5)
No	8371 (22.4)	29,162 (77.7)

[a] p value < 0.0001 between all groups for all characteristics using the χ^2 test.
[b] Noted percentage of the patients within each strata of characteristics presented.
[c] Some patients with data unavailable for specified characteristic.
HbA_{1C} = hemoglobin A_{1C}; SD = standard deviation.

Statistical Analysis

Contingency tables (χ^2) and differences in means (Student *t*-test) were used to evaluate differences in baseline characteristics across screening status categories and in pre-post analyses comparing health services use before and after symptom reporting. Among the subset of patients reporting symptoms, Cox proportional hazards models were used to assess whether the baseline demographic and clinical characteristics and health services use were associated with the primary outcomes of interest. The index date for these models was the first positive screen. All analyses were performed using statistical software (SAS Version 9.3, SAS Institute, Cary, NC).[16]

RESULTS

Characteristics of Screened Population

We identified 196,043 patients who met our inclusion criteria. Of these, 160,851 patients (85%) completed the DPN screen and were equally distributed across the 43 health care facilities in the Northern California Region (Figure 1). Patients who completed the questionnaire in the EMR were similar to those who were not screened in terms of sex, race, and ethnicity. However, patients who did not complete the questionnaire were slightly younger on average (mean age [standard deviation] = 58 [14] years) and were likelier to live in more socioeconomically deprived neighborhoods (55% vs 50% living in less socioeconomically deprived neighborhoods). Of those screened, 50,684 (31.5%) had a positive screen for DPN (Table 1). More than 99% of the population screened had a primary care physician. Among those screened, white patients (n = 25,557; 35.5%) were most likely to have reported DPN symptoms, and Asians were least likely (8129, 24%) to have reported DPN symptoms. With increasing deprivation or poverty per Census tract data, there was a small but significant increase in the proportion

of positive screens from 10,151 patients (29.7%) of the first quartile of poverty to 10,880 patients (33.0%) of the fourth quartile (most deprived; p < 0.0001). Patients with positive screens were more likely to report foot sores (n = 5194, 63.2%) compared with those with a negative screen (n = 30,124; 36.8%; p < 0.0001).

Changes in Health Services Use

Among patients with a positive screen, the proportion of patients with a DPN diagnosis increased from 30% at baseline to 45% after the screening (p < 0.05), whereas those with a negative screen saw an increase in DPN diagnoses of only 10% at baseline to 14% after screening (p < 0.05; difference in change after screen between groups = 11 %; p < 0.05; Table 2, Figure 2). In the subset of patients without a previous diagnosis, new DPN diagnoses were documented in 22% of patients with a positive screen compared with only 5% in those with a negative screen (difference in change between groups of 16.1%; p < 0.05; Figure 2). The proportion using any DPN medications increased by 8.2 percentage points after a positive screen compared with only 4.2 percentage points after a negative screen (difference in change after screen between groups = 4%; p < 0.05; Table 3).

Table 2 shows other changes in health services use stratified by screening status, including diagnoses for nondiabetic neuropathy conditions (difference in change between groups after screen = 9.8%, p < 0.05), neurology referrals (difference in change between groups in change after screen = 0.4%, p < 0.05), and podiatry referrals (difference in change between groups in change after screen = 2.7%, p < 0.05). There was no significant difference in the change in HbA_{1C} testing rates by positive vs negative screening status; however, greater than 90% of the population was already receiving HbA_{1C} testing.

Characteristics Associated with a DPN Diagnosis

The results of the Cox proportional hazards models estimating the likelihood of diagnosis, treatment initiation, and treatment intensification among those with a positive screen are shown in Table 4. Greater than 99% of all the clinical activity occurred on the day of the screening or soon after the screening. Thus, the predicted odds of clinical activity can be assumed to be the average odds of clinical activity during the year after each screening.[16] Older patients were more likely to receive a DPN diagnosis (45-64 years: hazard ration [HR] = 1.45, 95% confidence interval [CI] = 1.30-1.62; 65-74 years: HR = 1.79, 95% CI = 1.60-2.00; 75 years and older: HR = 1.69, 95% CI = 1.50-1.90). Also more likely to receive a DPN diagnosis were patients with elevated baseline HbA_{1C} (7%-9%: HR = 1.24, 95% CI = 1.19-1.31, > 9%: HR = 1.67, 95% CI = 1.56-1.78) and evidence of prior opioid use (HR = 1.18, 95% CI = 1.11-1.25).

Conversely, nonwhite patients were less likely to receive a DPN diagnosis: Black (HR = 0.88, 95% CI = 0.81-0.95), Hispanic (HR = 0.77, 95% CI = 0.72-0.82), Native American (HR = 0.74, 95% CI = 0.55-0.99), Pacific Islander (HR = 0.66, 95% CI = 0.51-0.86), Asian (HR = 0.59, 95% CI = 0.55-0.63), and mixed race (HR = 0.80, 95% CI = 0.72-0.90). In addition, patients with a greater number of primary care physician (PCP) visits were less likely to receive a DPN diagnosis (4-6 visits: HR = 0.86, 95% CI = 0.81-0.91; 7 or more visits: HR = 0.87, 95% CI = 0.82-0.92).

Table 2. Diabetic peripheral neuropathy (DPN) diagnoses, treatment, and health services use 12 months before and after DPN screen (April 2012-March 2014) stratified by screening status

	Positive screen for DPN, no. (%): 50,684 (31.5)		Negative screen for DPN, no. (%): 110,167 (68.5)		
Parameter	12 mo before	12 mo after	12 mo before	12 mo after	p value[a]
Number of primary care visits, mean (SD)	5.3 (6.5)	7.5 (7.1)	4.1 (5.4)	6.2 (6.2)	< 0.0001
DPN diagnosis					
Yes	15,080 (29.7)	22,749 (44.9)	10,712 (9.7)	15,630 (14.2)	< 0.0001
No	35,604 (70.3)	27,935 (55.1)	99,455 (90.3)	94,537 (85.8)	
Diagnosis of conditions with similar pain[b]					
Yes	16,568 (32.7)	24,396 (48.1)	14,300 (13.0)	20,450 (18.6)	< 0.0001
No	34,116 (67.3)	26,288 (51.9)	95,867 (87.0)	89,717 (81.4)	
HbA_{1C} test					
Yes	47,433 (93.6)	48,199 (95.1)	101,996 (92.6)	103,490 (93.9)	0.39
No	3251 (6.4)	2485 (4.9)	8171 (7.4)	6677 (6.1)	
Referral to specialist					
Endocrinologist	995 (2)	1414 (2.8)	1805 (1.6)	2529 (2.3)	0.12
Neurologist	1428 (2.8)	2222 (4.4)	1974 (1.8)	3340 (3.0)	0.01
Podiatrist	3341 (6.6)	5675 (11.2)	4084 (3.7)	6146 (5.6)	< 0.0001
Any DPN drug use					
Yes	9953 (19.6)	14,090 (27.8)	9058 (8.2)	13,637 (12.4)	< 0.0001
No	40,731 (80.4)	36,594 (72.2)	101,109 (91.8)	96,530 (87.6)	

[a] p value from the Cochran Mantel-Haenszel statistic, which tests if the postbaseline measures are equivalent between the positive and negative screen groups, after adjusting for prebaseline measures.

[b] International Classification of Diseases, Ninth Revision, codes for diagnoses with similar symptoms: 265, 266.0–266.9, 277.1, 277.3, 281.0, 281.1, 355.1, 355.5, 356.4, 357, 357.1, 357.3, 357.4, 357.5, 357.6, 357.7, 357.8, 357.9, 446.x, 714, 723.0, 724.00, 724.01, 724.02, 724.03, 724.09, 724.3, 443.9, 443.89.

HbA_{1C} = hemoglobin A_{1C}; SD = standard deviation.

Table 3. New diagnosis and related drug use relative to baseline over 12 months after screening

Parameter	Positive screen, no. (%): 50,684 (31.5)	Negative screen, no. (%): 110,167 (68.5)	p value[a]
New treatment started in patients without previous treatment	4137 (10.2)	4579 (4.5)	< 0.0001
New DPN diagnosis (no previous DPN diagnosis)			
Yes	7669 (21.5)	4918 (4.9)	< 0.0001
No	27,935 (78.5)	94,537 (95.1)	
Number of DPN drugs prescribed in patients without previous treatment[b]			
Mean (SD)	0.12 (0.37)	0.14 (0.41)	< 0.0001
Minimum-maximum	0-5	0-5	
Any treatment intensification in patients			
Yes	2293 (23.0)	1660 (18.3)	< 0.0001
No	7660 (77.0)	7398 (81.7)	

[a] p value from the χ^2 statistic.
[b] DPN treatment medications are amitriptyline, nortriptyline, imipramine, desipramine, duloxetine, paroxetine, citalopram, pregabalin, venlafaxine, or gabapentin.
DPN = diabetic peripheral neuropathy; SD = standard deviation.

Characteristics Associated with Treatment Initiation

Controlling for clinical and demographic factors, patients more likely to receive treatment after a positive DPN screen were women (HR = 1.33, 95% CI = 1.25-1.42), had an elevated HbA_{1C} of greater than 9% (HR = 1.22, 95% CI = 1.11-1.35), reported opioid use (HR = 1.69, 95% CI = 1.57-1.82), had a diagnosis with similar symptoms (HR = 1.35, 95% CI = 1.25-1.45), saw a neurologist (HR = 1.21, 95% CI = 1.01-1.46), and had a higher number of PCP visits (4-6 visits: HR = 1.20, 95% CI = 1.10-1.30; 7 or more visits: HR = 1.32, 95% CI = 1.22-1.43). However, patients of Asian race (HR = 0.67, 95% CI = 0.63-0.77) and those who lived in the least economically deprived neighborhoods (HR = 0.89, 95% CI = 0.80-0.99) were less likely to have treatment initiation after a positive screen.

Characteristics Associated with Treatment Intensification

Older patients were less likely to have treatment intensification: Specifically, those between ages 65 and 74 years (HR = 0.66, 95% CI = 0.52-0.83) and age older than 75 years (HR = 0.66, 95% CI = 0.52-0.83). Conversely, patients who were more likely to have treatment intensification after a positive screen were those with baseline opioid use (HR = 1.26, 95% CI = 1.15-1.37), other diagnoses with similar pain (HR = 1.26, 95% CI = 1.14-1.38), and any visit to a podiatrist (HR = 1.22, 95% CI = 1.07-1.39).

Treatment Change in Patients with Previous DPN Diagnoses

Subanalyses performed with the previously described Cox proportional hazards models in patients with a previous DPN diagnosis at the time of screening are presented in Table 5. As in the larger population, patients with prior opioid use (initiation: HR = 1.48, 95% CI = 1.31-1.67; intensification: HR = 1.24, 95% CI: 1.11-1.39) and increased number of PCP visits (> 7 visits: initiation: HR = 1.31, 95% CI = 1.14-1.50; intensification: HR = 1.40, 95% CI = 1.22-1.61) were more likely to have treatment initiation and intensification, respectively. However, among those who received a DPN diagnosis at the time of screening, older age, race, and socioeconomic status were not significantly associated with increased likelihood of new treatment or treatment intensification as it had in the larger population of patients who reported foot pain and paresthesias.

DISCUSSION

Among adults with diabetes, reporting DPN symptoms was associated with an increase in the intensity of DPN-related health care services use. Consistent with our hypothesis, there was an increase in the proportion of patients who received a DPN diagnosis. A positive screen was also associated with an increase in diagnoses for nondiabetic neuropathies. Rates of implementation of the survey were very high throughout the health system. This was likely aided by the integration of this short questionnaire into the EHR workflow of the medical assistants, which simplified its administration. However, the rates of treatment and referrals remained variable. This apparent lack of response may be owing to clinician concerns about the accuracy of the screen or the limited efficacy and adverse effects of available DPN treatments. In addition, since our screen question included

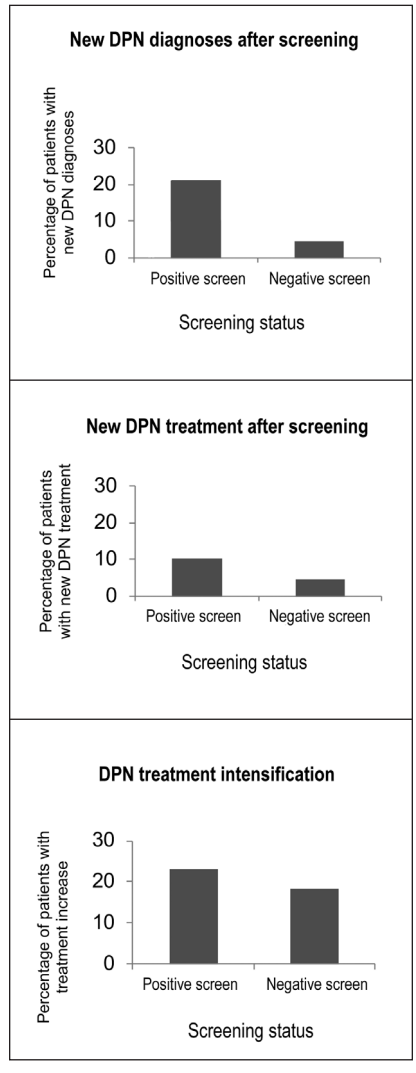

Figure 2. Intensification of DPN management by screening status among diabetic patients screened for DPN symptoms.
DPN = diabetic peripheral neuropathy.

both numbness and pain, treatment may not have been useful if the patient reported only numbness because the medications would not be effective. The lack of difference in HbA_{1C} testing rates between populations with a negative and a positive screen may reflect the already high testing rates. Interestingly, a higher number of primary care visits at baseline was associated with a decreased likelihood of new diagnoses, which may reflect underrecording of DPN diagnoses among patients with complex, competing health care needs. Patients with nondiabetic neuropathy diagnoses were more likely to have treatment initiation and intensification. This increase in clinical activity could be due to increased reporting of pain from conditions such as sciatica that are frequently more acute and self-limiting. Of note, neurologists may be more comfortable with starting patients on pain medication regimens compared with PCPs. However, intensification of preexisting pain medication regimens may not differ by specialty.

Our findings may, in part, reflect system-level factors that drive clinician response. For example, clinical practice guidelines at KPNC do not recommend nerve conduction studies because results do not change clinical management and could thus contribute to the low numbers of neurology referrals. Several clinical and demographic factors were associated with an increased likelihood of diagnosis and treatment, including opioid use, age, sex, race/ethnicity, and neighborhood deprivation index. Prior opioid use was associated with increased clinical activity throughout all the subgroup analyses, and this could be because of opioid use acting as an indicator of symptom severity warranting more clinical response or clinical complexity. Older patients were more likely to receive a diagnosis of DPN, but less likely to receive treatment intensification in response to a positive screen. This could reflect physician concerns regarding increased adverse drug events caused by DPN medications.[17-19]

Variation by race/ethnicity and sex are not well understood. Asian patients were less likely to receive a DPN diagnosis.

Table 4. Results of Cox proportional hazards models predicting patient characteristics associated with clinical response among patients with a positive screen over 12 months after screening[a]

	Likelihood of diagnosis (n = 35,604)		Likelihood of new treatment (n = 40,731)		Likelihood of treatment intensification (n = 9953)	
Characteristic (reference)	Hazard ratio	95% CI	Hazard ratio	95% CI	Hazard ratio	95% CI
Age, y (reference < 45 y)						
45-64	1.45	**1.30-1.62**	1.13	0.97-1.30	0.84	0.68-1.04
65-74	**1.79**	**1.60-2.00**	0.97	0.83-1.14	**0.63**	**0.50-0.78**
≥ 75	**1.69**	**1.50-1.90**	0.96	0.81-1.13	**0.66**	**0.52-0.83**
Sex						
Female (male)	**0.88**	**0.84-0.92**	**1.33**	**1.25-1.42**	1.05	0.96-1.14
Race (white)						
Black	**0.88**	**0.81-0.95**	0.95	0.85-1.06	1.00	0.86-1.16
Hispanic	**0.77**	0.72-0.82	1.04	0.95-1.14	0.97	0.85-1.10
Native American	**0.74**	**0.55-0.99**	0.94	0.64-1.37	1.04	0.68-1.58
Pacific Islander	**0.66**	**0.51-0.86**	1.19	0.88-1.63	0.59	0.28-1.24
Asian	**0.59**	**0.55-0.63**	**0.67**	**0.63-0.77**	0.92	0.77-1.09
Mixed	**0.80**	**0.72-0.90**	1.05	0.91-1.22	0.96	0.80-1.15
Neighborhood deprivation index (fourth quartile)						
First quartile (least deprived)	1.03	0.96-1.10	**0.89**	**0.80-0.99**	1.00	0.88-1.15
Second quartile	0.10	0.94-1.06	0.96	0.88-1.06	0.97	0.86-1.09
Third quartile	1.01	0.95-1.08	0.97	0.89-1.06	0.96	0.98-1.24
HbA_{1C} (< 7% [53 mmol/mol])						
7%-9% (53-75 mmol/mol)	1.24	1.19-1.31	1.05	0.98-1.13	0.93	0.85-1.02
> 9% (75 mmol/mol)	1.67	1.56-1.78	1.22	1.11-1.35	1.05	0.92-1.19
Visits to primary care physician at baseline (< 4)						
4-6	**0.86**	**0.81-0.91**	**1.20**	**1.10-1.30**	1.10	0.98-1.24
7 or more	**0.87**	**0.82-0.92**	**1.32**	**1.22-1.43**	1.38	1.24-1.53
Any visit to specialist						
Endocrinologist	1.10	0.92-1.30	0.95	0.75-1.19	1.02	0.81-1.27
Neurologist	0.93	0.78-1.10	**1.21**	**1.01-1.46**	1.04	0.88-1.24
Podiatrist	0.95	0.85-1.07	1.11	0.99-1.25	**1.22**	**1.07-1.39**
Other						
Opioid use	**1.18**	**1.11-1.25**	**1.69**	**1.57-1.82**	**1.26**	**1.15-1.37**
Nondiabetic neuropathy diagnosis	0.95	0.86-1.03	**1.35**	**1.25-1.45**	**1.26**	**1.14-1.38**

[a] Bold values denote statistical significance at p value < 0.05.
CI = confidence interval; HbA_{1C} = hemoglobin A_{1C}.

Table 5. Results of Cox proportional hazards models predicting physician 12-month follow-up to patient reports of diabetic peripheral neuropathy (DPN) symptoms in subset of patients with positive screen and previous DPN diagnosis before screen[a]

	Time to prescription		Time to prescription intensification	
Characteristic (reference)	Hazard Ratio	95% CI	Hazard Ratio	95% CI
Age, y (reference < 45 y)				
45-64	1.03	0.72, 1.49	0.94	0.68, 1.30
65-74	0.98	0.68, 1.42	0.72	0.52, 1.01
75+	0.96	0.66, 1.40	0.78	0.56, 1.09
Sex				
Female (male)	**1.27**	**1.13, 1.42**	1.11	0.99, 1.24
Race (white)				
Black	0.87	0.71, 1.05	0.95	0.78, 1.15
Hispanic	1.13	0.96, 1.33	1.08	0.91, 1.27
Native American	1.06	0.57, 1.99	0.87	0.50, 1.51
Pacific Islander	1.62	0.89, 2.95	0.80	0.33, 1.94
Asian	0.84	0.69, 1.02	1.08	0.87, 1.34
Mixed	1.20	0.95, 1.51	1.07	0.86, 1.33
Neighborhood deprivation index (fourth quartile)				
First quartile (least deprived)	0.85	0.72, 1.02	1.02	0.85, 1.21
Second quartile	**0.82**	**0.70, 0.97**	0.97	0.83, 1.14
Third quartile	0.92	0.79, 1.07	0.90	0.77, 1.05
HbA_{1C} [<7% (53 mmol/mol)]				
7-9% (53-75 mmol/mol)	1.04	0.91, 1.18	0.99	0.88, 1.12
>9% (75 mmol/mol)	1.15	0.96, 1.36	1.05	0.89, 1.25
Visits to primary care physician at baseline				
4-6	**1.23**	**1.06, 1.43**	1.08	0.92, 1.27
7 or more	**1.31**	**1.14, 1.50**	**1.40**	**1.22, 1.61**
Any visit to specialist				
Endocrinologist	1.11	0.82, 1.52	1.12	0.87, 1.45
Neurologist	1.06	0.82, 1.38	1.08	0.89, 1.32
Podiatrist	**1.26**	**1.08, 1.48**	**1.24**	**1.08, 1.44**
Other				
Opioid use	**1.48**	**1.31, 1.67**	**1.24**	**1.11, 1.39**
Nondiabetes neuropathy diagnosis	1.13	0.88, 1.46	0.98	0.77, 1.24

[a] Bold values denote statistical significance at p value < 0.05.
CI = confidence interval; HbA_{1C} = hemoglobin A_{1C}.

However, as suggested by subanalysis of the group of patients with DPN diagnoses, the rates of treatment were equal among the races after receiving a DPN diagnosis. The lack of racial variation in treatment after a positive symptom screen overall suggests that the cause of foot pain in the nonwhite population may point to a non-DPN diagnosis that we did not capture. It is unclear if variation in diagnosis is caused by differences in reporting of symptoms by race/ethnicity, sex, and socioeconomic status or prevalence of DPN in these populations as described in prior studies.[20]

There are several limitations to this study that warrant discussion. First, this study was conducted in a single health care system and may not reflect general practice in a noncapitated system. However, prior research[21,22] showing undertreatment of DPN in primary care settings and the diversity of our population suggest that our findings may, in fact, be generalizable. In addition, the screen implemented in this setting has not been previously validated and may be less accurate than other previously validated instruments.[10-12] Furthermore, there is limited incentive for clinicians to record DPN diagnoses in the EMR in this capitated care system that has vertical integration between clinicians and the insurer. Also, even though a variety of ICD-9 codes were used to assess for a DPN diagnosis, it is possible that other ICD-9 codes are used in clinical practice in these various clinics because of differences in practice styles that may not have been included. In addition, we examined indicators of clinician response contained in coded fields and did not include other indications such as physical examinations and communication with patients about symptoms.

Because the intervention was limited to an in-person visit, patients who did not have in-office visits, such as virtual visits, were not privy to the intervention. In addition, there is limited incentive to code DPN in the inpatient setting during acute care episodes. Therefore, it is likely that we have underestimated the number of diagnoses. This study centered around an intervention in the primary care setting, so we did not capture all possible health system interactions such as direct podiatry visits without referral that may have happened outside the primary care visit. However, we did endeavor to capture all actions generated by PCPs, as this was the focus of the screener intervention. In addition, despite our efforts to exclude some subsets of patients from analysis on the basis of the comorbidity, the rates of treatment may not reflect appropriate care for all included patients. We may have overestimated the rates of treatment given that medications used to treat DPN are also used to treat a number of other conditions (eg, depression, seizure disorders).[1] Conversely, we did not count prescriptions that were already prescribed for another condition. Also, because our screening question included both pain and numbness, the change in treatment strategies could be limited because numbness is not treated with the medications we included as part of this study. This study was limited to the first screening of each patient, and further study could be focused on changes in clinical activity after multiple symptom screenings over time.

As mentioned earlier, the proportional hazards assumption for the regression model used in this study was not met because most of the clinical activity occurred during the screening visit itself. However, because the

time-related interactions were not very strong, suppressing these interactions would not lead to additional bias in the model.

Strengths of this analysis included our ability to link patient-reported symptoms with rich electronic health data. To our knowledge, this is one of a few studies that have been able to rigorously assess changes in DPN management in response to patient reports of symptoms.

CONCLUSION

We found that a single question assessing DPN symptoms from a 4-question screen for diabetic complications was associated with increased rates of DPN diagnoses in the EMR. However, significant changes in treatment and general DPN management were slower to emerge and may have been related to physician concerns about the efficacy and tolerability of treatment, particularly among older patients, and system-level factors related to low use of monofilament testing. Future studies might assess whether interventions combining a brief screener with monofilament testing among patients at highest risk of adverse events might have greater impact on clinical practice. However, such effort would need to consider notable variation in diagnosis rates by race/ethnicity and sex that may reflect differences in patient presentation or clinician interpretation of symptoms. It is interesting to note that, in this health system, the likelihood of treatment after a DPN diagnosis did not vary with race, age, and socioeconomic status. Although this tool was useful for capturing patient-reported information about DPN symptoms in real time, additional decision aids may be required to overcome diagnostic and treatment challenges to ensure that timely treatment occurs. A simple 1-question screen for symptoms can be a triage tool for intensification of clinical services for patients with DPN. ❖

Disclosure Statement

The author(s) have no conflicts of interest to disclose.

Author Contributions

Melissa M Parker, MS, contributed to the data collection and statistical analyses and reviewed and edited the manuscript. Somalee Banerjee, MD, MPH, and Alyce Adams, PhD, wrote the manuscript and edited and interpreted the data. Alyce Adams, PhD, also provided the funding and data. Eileen Kim, MD; Rick Dlott, MD; and Lisa K Gilliam, MD, PhD, reviewed and edited the manuscript.

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