

BURDEN OF ILLNESS ASSOCIATED WITH SYMPTOMS OF DIABETIC PERIPHERAL NEUROPATHY AND DIABETIC RETINOPATHY

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ABSTRACT

OBJECTIVES: To evaluate the effect of symptoms characteristic of diabetic peripheral neuropathy (SDPN), diabetic retinopathy (DR) and co-morbid SDPN & DR (COMORB) among US adults =40 years old with diagnosed diabetes on several burden of illness (BOI) measures, including indirect costs and healthcare utilization, using the combined 1999-2000 and 2001-2002 National Health and Nutrition Examination Surveys (NHANES).

METHODS: Included in the analysis were 850 NHANES respondents =40 years old classified as having diagnosed diabetes. Logistic regression models were used to assess the effect of SDPN, DR and COMORB on BOI. Model covariates included age, gender, race, education, insurance status, current smoking status, currently asthmatic, and history of cardiovascular disease, cancer, arthritis, COPD, hypertension and stroke. The conditions of interest were assessed based upon respondent self-report.

RESULTS: Using the combined 1999-2000 and 2001-2002 NHANES, it was estimated that, among US adults aged =40 years old with diagnosed diabetes, those with SDPN (OR = 2.27; 95%CI = 1.34, 3.85), DR (1.67; 1.08, 2.59) and COMORB (2.88; 1.28, 6.48) were each more likely to have 4 or more healthcare visits in the past year than those without the corresponding condition. Those with DR (1.81; 1.31, 2.50) and COMORB (2.07; 1.13, 3.77) were both more likely to have had at least one overnight hospital stay in the past year. Finally, those of working age (40-65) with SDPN (3.31; 1.64, 6.64), DR (2.99; 1.47, 6.08) and COMORB (4.40; 2.22, 8.74) were each more likely to be unable to work due to physical limitations.

CONCLUSION: Among US adults aged =40 years old with diagnosed diabetes, SDPN, DR, and COMORB all appear to significantly increase BOI. Future therapies that offer relief of both of these conditions may have significant benefits on direct measures of healthcare resource utilization and indirect costs (such as lost work time).

Introduction

Despite the development of comprehensive diabetes management programs over the past 2 decades, many patients with diabetes continue to be at an increased risk for diabetic microvascular complications such as diabetic peripheral neuropathy (DPN) and diabetic retinopathy (DR). DPN and DR are significant problems that negatively impact the quality of life of diabetes patients. Moreover, significant healthcare resources are spent each year to treat these conditions, both for active symptoms and for late-stage complications including ulcers and amputations.

Although often diagnosed and treated separately, DPN and DR are pathologically linked. Previous research (Dyck et al., 1999, for example) has identified three lines of evidence suggesting that DPN and DR have a similar metabolic genesis: 1) DPN and DR are statistically associated; 2) microvascular changes are histologically and functionally similar in vessels taken from areas affected by either condition; and 3) prospective studies evaluating improved hyperglycemic control results in a similar preventive effect on both conditions.

Objective

The objective of this study was to estimate the prevalence and associated burden of illness of symptoms characteristic of diabetic peripheral neuropathy (SDPN) and diabetic retinopathy (DR) among US adults aged 40 and older with diagnosed diabetes.

Data Sources

NHANES is a nationally representative, periodic survey of the non-institutionalized US civilian population, and is administered by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). NHANES staff conduct interviews and perform physical examinations on participants. Respondents are interviewed in their homes to obtain information on health history, behaviors, and risk factors. Respondents are also asked to undergo a physical examination in a mobile examination center. The procedures used to select the sample and to conduct the interview and examination have been described in great detail in the literature (CDC, 2002).

For this study, we analyzed the combined NHANES 1999-2000 and 2001-2002.

Methods

In this study, we analyzed NHANES data to assess differences in the rate at which patients with and without SDPN, DR and comorbid SDPN and DR consume healthcare resources (e.g., visit their healthcare provider, spend the night in a hospital). For example, we examined whether or not those with comorbid SDPN and DR are more likely to have 4 or more healthcare visits in the past year than those without both conditions.

Analyses were conducted using SAS for Windows statistical software (Version 8.2). Final results included both unweighted and weighted (e.g., nationally representative) estimates. Following Gregg et al. (2004), we did not undertake any form of imputation to account for missing data. Using the sampling weights provided with the NHANES releases, we were able to generate nationally representative prevalence estimates.

We supplemented demographic information with data from the Diabetes questionnaire. Respondents 20+ years of age were asked about history of retinopathy and vision troubles due to diabetes, while respondents 40+ years of age were asked about history of numbness in hands or feet. Thus, our analytic sample was limited to adults 40+ years of age.

From the original NHANES sample of adults 40 years of age and older, we excluded respondents for the following reasons:

• Did not complete the exam and therefore would not have certain key information (e.g., monofilament testing results, plasma glucose), and
• Were not part of the Peripheral Neuropathy Section of the Lower Extremity Disease examination. Persons are excluded from this exam if they are younger than 40 years of age, have bilateral amputations, or weigh over 400 pounds.

Diabetes-related Variables

We classified a respondent as having been diagnosed with diabetes if:
• He or she answered yes to the question "Doctor told you have diabetes?", or
• He or she reports currently taking insulin or diabetic pills for diabetes.

We classified a respondent as having SDPN if:

• He or she reports numbness, loss of feeling, or painful sensations or feeling in their feet.

We classified a respondent as having DR if:

• He or she answered yes to the question "Has diabetes affected your eyes/do you have retinopathy?"

We classified a respondent as having comorbid SDPN and DR if they were classified as having both conditions, as defined above.

Burden of Illness Variables

Number of healthcare visits in the past 12 months: We assessed the number of times a respondent reported visiting a healthcare provider during the past 12 months using response to the question "During the past 12 months, how many times have you seen a doctor or other health care professional about your health at a doctor's office, a clinic, hospital emergency room, at home or some other place? Do not include times hospitalized overnight."

Mental health visit in the past 12 months: We classified a respondent as having visited a mental health professional in the past 12 months if s/he responded positively to the question "During the past 12 months, have you seen or talked to a mental health professional such as a psychologist, psychiatrist, psychiatric nurse or clinical social worker about your health?"

Overnight hospital stay in the past 12 months: We classified a respondent as having had (any) overnight hospital stay in the past 12 months if s/he responded positively to the question "During the past 12 months, were you a patient in a hospital overnight? Do not include an overnight stay in the emergency room."

Number of overnight hospital stays in the past 12 months: We assessed the number of times a respondent reported having an overnight hospital stay in the past 12 months using response to the question "During the past 12 months, how many times were you an overnight hospital patient?" Number of prescription medicines reported: We assessed the number of prescription medicines a respondent reported taking using the variable.

Inability to work: We classified a respondent as being unable to work due to a health concern if s/he responded positively to the question "Does a physical, mental or emotional problem now keep you from working at a job or business?"

Limited ability to work: We classified a respondent as being limited in his or her ability to work due to a health concern if s/he responded positively to the question "Are you limited in the kind or amount of work you can do because of a physical, mental or emotional problem?"

In addition, we created a number of variables to describe the burden of illness which were based upon the previously defined variables. These new measures included dichotomous terms for:

- Had 3 or more overnight hospital stays in past year?
- Had 4 or more healthcare visits in past year?

Models Estimated

Using Stata's SVYREG command, which adjusts for NHANES' complex survey design, we estimated ordinary least squares regression models of the general form:

$$BOI_i = \beta_0 + \beta_1COND_i + \beta_2X_i + \epsilon_i$$

where BOI_i is a continuous burden of illness outcome (e.g., number of prescription medications currently being taken), COND is a condition indicator (SDPN, DR, or comorbid SDPN and DR), X is a vector of explanatory variables, and ϵ_i is the error term.

Explanatory variables included: age, gender, race (non-white is the reference category), current smoker status, education (high school graduate and above is the reference category), self-reported cardiovascular disease, cancer, arthritis, chronic obstructive pulmonary disease, hypertension, stroke, currently asthmatic, and insurance status (no insurance is the reference category).

Using Stata's SVYLOGIT command, which adjusts for NHANES' complex survey design, we estimated logistic regression models of the general form:

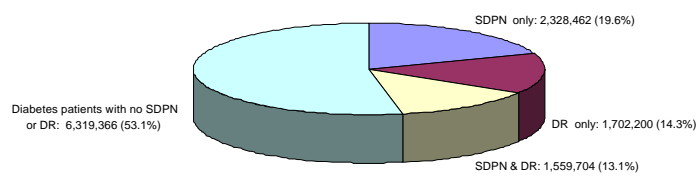
$$BOI_i = \beta_0 + \beta_1COND_i + \beta_2X_i + \epsilon_i$$

where BOI_i is a dichotomous outcome of interest (e.g., had at least one mental health visit in the past 12 months or had at least one overnight hospital stay in the past 12 months), COND is a condition indicator (SDPN, DR, or comorbid SDPN and DR), X is a vector of explanatory variables, and ϵ_i is the error term.

Explanatory variables included: age, gender, race (non-white is the reference category), current smoker status, education (high school graduate and above is the reference category), self-reported cardiovascular disease, cancer, arthritis, chronic obstructive pulmonary disease, hypertension, stroke, currently asthmatic, and insurance status (no insurance is the reference category).

In addition, using the same vector of explanatory variables listed above, we used Stata's SVYMLLOGIT command, which adjusts for NHANES' complex survey design, to estimate multinomial logit regression models to estimate the number of overnight hospital stays, as well as the number of healthcare visits in the past 12 months. As recorded in NHANES, these variables are not strictly continuous (i.e., 0, 1, 2-3, 4-9, 10-12, and 13 or more for the number of healthcare visits in the past 12 months).

Distribution of SDPN and DR Among Diabetes Patient in the U.S. (>= 40 years of age)



Distribution of Demographic Factors

AGE CATEGORY	SYMPTOMS OF DPN (SDPN) ^a				YES			
	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)
40-49	74	1,678,110	20.92	77.69	35.00	481,834	12.39	22.31
50-59	92	1,853,345	23.10	63.07	51.00	1,084,987	27.90	36.93
60-69	196	2,111,564	26.32	61.63	107.00	1,314,472	33.81	38.37
70-79	127	1,535,638	19.14	66.1	70.00	787,483	20.25	33.60
80+	72	842,909	10.51	79.35	26.00	219,390	5.64	20.65
GENDER								
MALE	291	4,131,687	51.51	69.05	140.00	1,852,163	47.64	30.95
FEMALE	270	3,889,879	48.49	65.64	149.00	2,036,004	52.36	34.36
ELDERLY^b								
ELDERLY (>=65)	266	4,591,988	57.25	67.61	145.00	2,199,916	56.58	32.39
NON-ELDERLY (<65)	295	3,429,578	42.75	67.01	144.00	1,688,251	43.42	32.99
RACE/ETHNICITY								
NON-HISPANIC WHITE	207	5,113,991	63.75	68.26	99.00	2,378,353	61.17	31.74
NON-HISPANIC BLACK	139	1,152,171	14.36	61.61	77.00	717,884	18.46	38.39
MEXICAN AMERICAN	163	541,823	6.75	66.91	87.00	267,985	6.89	33.09
OTHER RACE, INCLUDING MULTI-RACIAL	17	465,665	5.81	71.19	8.00	188,476	4.85	28.81
OTHER HISPANIC	35	747,917	9.32	69.04	18.00	335,469	8.63	30.96
LESS THAN HIGH SCHOOL EDUCATION								
NO	265	4,968,167	61.94	66.78	138.00	2,471,744	63.57	33.22
YES	296	3,053,399	38.06	68.31	151.00	1,416,422	36.43	31.69
ANY INSURANCE COVERAGE^c								
NO	63	664,523	8.28	55.14	49.00	540,724	13.91	44.86
YES	498	7,357,043	91.72	68.73	240.00	3,347,442	86.09	31.27
TOTAL	561	8,621,566	100.00	67.35	289.00	3,888,166	100.00	32.65

AGE CATEGORY	DIABETIC RETINOPATHY ^a				YES			
	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)
40-49	76	1,628,292	18.83	75.39	33.00	531,652	16.30	24.61
50-59	109	2,212,006	25.58	75.28	34.00	726,325	22.27	24.72
60-69	209	2,340,345	27.06	68.31	94.00	1,085,691	33.28	31.69
70-79	128	1,658,843	19.18	71.41	69.00	664,278	20.36	28.59
80+	76	808,341	9.35	76.09	22.00	253,958	7.79	23.91
GENDER								
MALE	303	4,470,815	51.70	74.71	128.00	1,513,034	46.38	25.29
FEMALE	295	4,177,013	48.30	70.49	124.00	1,748,870	53.62	29.51
ELDERLY^b								
ELDERLY (>=65)	295	5,074,259	58.68	74.71	116.00	1,717,645	52.66	25.29
NON-ELDERLY (<65)	303	3,573,569	41.32	69.83	136.00	1,544,259	47.34	30.17
RACE/ETHNICITY								
NON-HISPANIC WHITE	233	5,736,303	66.33	76.56	73.00	1,756,041	53.83	23.44
NON-HISPANIC BLACK	142	1,235,153	14.28	66.05	74.00	634,901	19.46	33.95
MEXICAN AMERICAN	170	566,503	6.55	69.96	80.00	243,305	7.46	30.04
OTHER RACE, INCLUDING MULTI-RACIAL	15	400,632	4.63	61.25	10.00	253,509	7.77	38.75
OTHER HISPANIC	38	709,237	8.20	65.46	15.00	374,149	11.47	34.54
LESS THAN HIGH SCHOOL EDUCATION								
NO	295	5,508,895	63.70	74.05	108.00	1,931,016	59.20	25.95
YES	303	3,136,933	36.30	70.23	144.00	1,339,888	40.80	29.77
ANY INSURANCE COVERAGE^c								
NO	85	991,105	11.23	80.57	27.00	234,142	7.18	19.43
YES	513	7,676,723	88.77	71.72	235.00	3,627,262	92.82	28.28
TOTAL	598	8,647,828	100.00	72.61	252.00	3,261,204	100.00	27.39

Results

Distribution of Demographic Factors (cont.)

AGE CATEGORY	CO-MORBID DR AND SDPN				YES			
	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)	UNWEIGHTED n	WEIGHTED % (COL)	UNWEIGHTED n	WEIGHTED % (ROW)
40-49	93	1,953,791	18.88	90.46	16.00	206,154	13.22	9.54
50-59	125	2,591,383	25.04	88.19	18.00	346,948	22.24	11.81
60-69	255	2,795,679	27.01	81.6	48.00	630,356	40.42	18.40
70-79	162	2,007,264	19.39	86.4	35.00	315,857	20.25	13.60
80+	91	1,001,910	9.68	94.32	7.00	60,389	3.87	5.68
GENDER								
MALE	370	5,291,051	51.12	88.42	61.00	692,799	44.42	11.58
FEMALE	356	5,058,977	48.88	85.37	63.00	866,906	55.58	14.63
ELDERLY^b								
ELDERLY (>=65)	350	5,998,965	57.96	88.33	61.00	792,939	50.84	11.67
NON-ELDERLY (<65)	376	4,351,063	42.04	85.02	63.00	766,766	49.16	14.98
RACE/ETHNICITY								
NON-HISPANIC WHITE	272	6,680,329	64.54	89.16	34.00	812,015	52.06	10.84
NON-HISPANIC BLACK	177	1,521,149	14.70	81.34	39.00	348,905	22.37	18.66
MEXICAN AMERICAN	211	694,772	6.71	85.79	39.00	115,036	7.38	14.21
OTHER RACE, INCLUDING MULTI-RACIAL	21	544,494	5.26	83.24	4.00	109,647	7.03	16.76
OTHER HISPANIC	45	909,285	8.79	83.93	8.00	174,011	11.16	16.07
LESS THAN HIGH SCHOOL EDUCATION								
NO	350	6,521,297	63.01	87.65	53.00	918,614	58.90	12.35
YES	376	3,828,731	36.99	85.66	71.00	641,090	41.10	14.34
ANY INSURANCE COVERAGE^c								
NO	94	1,031,879	9.97	85.62	18.00	173,368	11.12	14.38
YES	632	9,318,149	90.03	87.05	106.00	1,386,336	68.88	12.95
TOTAL	726	10,350,028	100.00	86.9	124.00	1,559,704	100.00	13.10

Modeling Estimates

Outcome Modeled	Parameter of Interest ^{1,2}	Odds Ratio ³	95% CI ⁴
Unable to work due to physical limitations ⁵	SDPN**	3.31	1.64
	Retinopathy**	2.99	1.47
	Comorbid SDPN and DR**	4.40	2.22
At least 1 overnight hospital stay in past year	SDPN	1.45	0.80
	Retinopathy**	1.81	1.31
	Comorbid SDPN and DR*	2.07	1.13
Had 4 or more healthcare visits in past year	SDPN*	2.27	1.34
	Retinopathy*	1.67	1.08
	Comorbid SDPN and DR*	2.88	1.28
Visited a mental health professional in past year	SDPN	1.68	0.90
	Retinopathy	1.51	0.74
	Comorbid SDPN and DR*	1.90	1.03
Outcome	Comparative Groups		