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ORIGINAL RESEARCH

Incidence of diabetic peripheral neuropathic pain in primary care – a retrospective cohort study using the United Kingdom General Practice Research Database

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Purpose: To determine the incidence of diabetic peripheral neuropathic pain (DPNP) in the United Kingdom (UK) primary care population using the General Practice Research Database (GPRD).

Patients and methods: This retrospective cohort study identified incident cases of DPNP in the UK GPRD between July 1, 2002 and June 30, 2011, using diagnostic codes. Trends in the incidence rate were examined by dividing the study period into 3-year periods: (1) July 1, 2002–June 30, 2005; (2) July 1, 2005–June 30, 2008; and (3) July 1, 2008–June 30, 2011. Patient characteristics (age, sex, comorbidities) and initial pharmacological treatment were described; the proportion of patients with incident DPNP, who had previously been screened for neuropathic symptoms, was determined.

Results: Among almost 7.5 million persons contributing 38,118,838 person-years of observations in the GPRD, 6,779 new cases of DPNP were identified (45.5%, women), giving an incidence rate of 17.8 per 100,000 person-years (95% confidence interval [CI] 17.4–18.2). The incidence of DPNP increased with age, but it was stable over the three consecutive 3-year periods: 17.9, 17.2, and 18.4 cases per 100,000 person-years. Of the 6,779 patients with incident DPNP, 15.5% had prior neuropathic screening during the study period. The majority of patients with incident DPNP (84.5%) had a treatment for pain initiated within 28 days of first diagnosis. The most common first-line treatments prescribed were tricyclic antidepressants (27.2%), anticonvulsants (17.0%), and nonsteroidal anti-inflammatory drugs (14.9%), with 26.6% of patients receiving combination therapy as their initial treatment.

Conclusion: The incidence of DPNP in UK primary care has remained steady over the past 10 years. Our results suggest that DPNP is underdiagnosed, and initial treatment prescribed does not follow clinical guidelines.

Keywords: diabetes, peripheral neuropathy, pain, incidence, primary care

Introduction

Peripheral neuropathy affects up to 50% of patients with diabetes and is characterized by pain, paresthesia, and sensory loss, increasing the risk for foot problems that can result in amputation.[1] Diabetic peripheral neuropathic pain (DPNP) is generally diagnosed and managed in the primary care setting in the United Kingdom (UK), but it can be difficult for general practitioners (GPs) to recognize, because patients often do not relate pain to diabetes and, therefore, do not volunteer information on their pain symptoms during consultations.[2] DPNP is associated with impaired patient functioning and quality of life,

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as well as higher societal and health care costs compared to patients with diabetes but without neuropathic pain.[3,4]

Prevalence rates of DPNP in Europe range from 8%–26% in different diabetes patient populations.[5–11] In the UK, the prevalence of DPNP in the diabetes population ranges from 10%–26%, depending on the criteria used to assess/define DPNP and the patient population studied.[5–7]

Incidence of DPNP has been less well-studied, but it is an important measure within the general population to inform health policy for screening and detection and to plan health care resources. A study, using the UK General Practice Research Database (GPRD), estimated the incidence of DPNP at 15.3 cases per 100,000 person-years in the UK primary care population between 1992 and 2002,[12] increasing to 27.2 cases per 100,000 person-years between 2002 and 2005.[13]

In the UK, clinical practice guidelines for patients with diabetes include annual checks for neuropathic symptoms and appropriate pain management plans to improve patient outcomes.[2,14] Annual screening of all diabetes patients for neuropathy and a foot examination (including assessment of peripheral pulses and sensation) is part of the Quality Outcome Framework (QOF), a financial incentive scheme for GP practices introduced in 2004.[15]

Up-to-date DPNP incidence rates will inform health care providers and practitioners on the impact of clinical guidelines and neuropathic screening on the diagnosis and treatment patterns of DPNP in UK primary care; such information is captured in the GPRD.

The objectives of our study were to use the GPRD to determine the impact of the introduction of national guidelines[14] on the incidence of DPNP in the UK primary care population in the last 9 years and to examine trends in the incidence rate over the study period (2002–2011). In addition, we describe the characteristics of the primary care patients with incident DPNP and their initial pharmacological treatment, and we determined the proportion of patients with incident DPNP who had previously been screened for neuropathic symptoms.

Material and methods

Data source

This study used a retrospective cohort design to identify incident cases of DPNP in the UK GPRD between July 1, 2002–June 30, 2011. GPRD records for >5 million currently registered patients meet the GPRD standards of acceptable quality for use in research, which is equivalent to approximately 8.5% of the UK population.[16] Recent systematic reviews have confirmed the validity of medical diagnoses and quality of information on the GPRD.[17,18]

Study population and study cohort with incident DPNP

The total study population included all patients who were permanently registered at one of the GP practices contributing to the GPRD system at any time during the 9-year study period (July 1, 2002–June 30, 2011) and who provided acceptable-quality data as recorded in the GPRD. For each patient, the period of observation was from a start date to an end date. The start date was defined as the last of either: (1) the start of the study period (July 1, 2002); (2) the patient's date of registration with the practice; or (3) the date the practice was considered "up to standard" by the GPRD. The end date was defined as the first of the following: (1) end of the study period (June 30, 2011); (2) death; (3) transfer out of the practice; or (4) the final data collection.

The study cohort with incident DPNP was identified from the total population and included those who had a GPRD record containing one of the following: a diagnosis of DPNP; a diagnosis of diabetic neuropathy with a prescription for treatment for pain current at the date of diagnosis; a diagnosis of diabetes and neuropathic pain; and a diagnosis of both diabetes and neuralgia plus a treatment for pain current on the data of the neuralgia code. Prescription for treatment for pain includes antidepressants, anticonvulsants, narcotics, nonnarcotics, and nonsteroidal anti-inflammatory drugs (NSAIDs). All diagnoses were identified based on Read codes (Table S1 and Table S2). Patients were excluded from the study cohort if they had a DPNP diagnosis in their record prior to the incident date, which was defined as the date of the first DPNP diagnosis recorded in the GPRD during the study period. They were also excluded if they had fewer than 12 months of computerized data prior to the incident date or data not considered of acceptable quality by the GPRD.

Figure 1 presents the flow chart for identification and selection of the study cohort with incident DPNP in the GPRD.

Data collected

Data on patient age and sex were collected from the GPRD for the total eligible population (n = 7,483,143) and for the study cohort with incident DPNP (n = 6,779).

For the study cohort, information was collected on the most common diabetes-related comorbidities (cardiovascular disease, cerebrovascular and peripheral vascular disease, retinopathy, hypoglycemic event, other metabolic

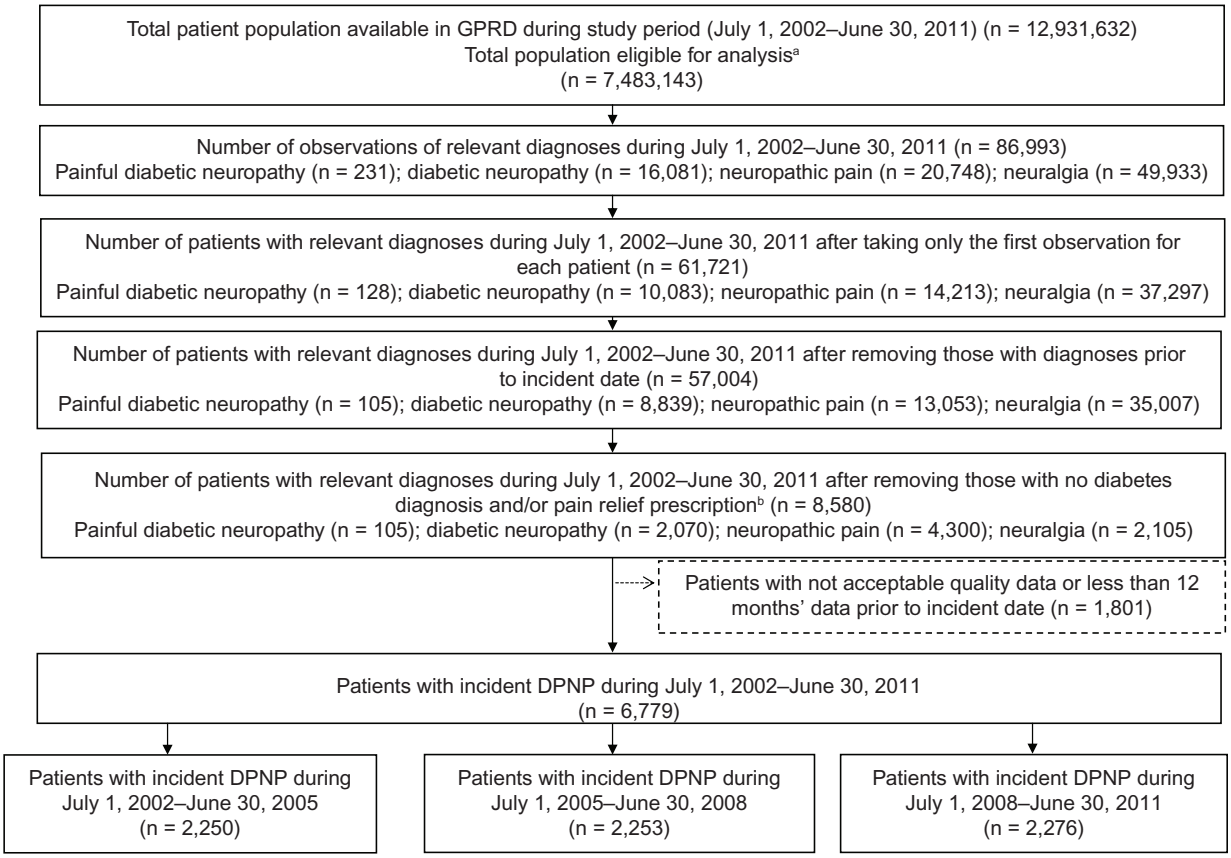

Figure 1 Flow diagram of selection of patient cohort from GPRD.
Notes: [a]Those who had acceptable quality data and were registered at any time during the total study period (July 1, 2002–June 30, 2011); [b]Patients with the following conditions were removed: patients with diabetic neuropathy but no pain relief prescriptions on the date of diabetic neuropathy code; patients with neuropathic pain but no diagnosis of diabetes recorded between July 1, 2002 and June 30, 2011; patients with neuralgia but no diagnosis of diabetes recorded between July 1, 2002 and June 30, 2011 and/or no pain relief prescriptions on the data of neuralgia code.
Abbreviations: GPRD, General Practice Research Database; DPNP, diabetic peripheral neuropathic pain; n, number.

diseases, skin problems, nephropathy, obesity, and anxiety) and pain-related comorbidities (lower back pain, osteoarthritis, fibromyalgia syndrome, migraine, psoriatic arthropathy, and rheumatoid arthritis). Items from the Charlson Comorbidity Index (CCI) were identified using 17 previously defined categories of comorbid conditions based on Read codes.[19] The frequency and percentage of these comorbidities in the 12 months before the incident date were estimated; and the CCI score, a summary measure of index that represents the 1-year mortality for patients based on their history of a range of comorbid conditions, was calculated for each patient.

Information on initial treatment for DPNP was collected within 28 days of the first record of the DPNP diagnosis (incident date) during the study period for: tricyclic antidepressants (TCAs); selective serotonin reuptake inhibitors (SSRIs); serotonin norepinephrine reuptake inhibitors (SNRIs); other antidepressants; anticonvulsants; opioids; nonnarcotics; and NSAIDs. The frequency and percentage of each type of drug were estimated. If more than one pharmacotherapy was prescribed on the same day, the initial treatment was considered to be a combination of these therapies.

The frequency and percentage of patients who underwent screening for neuropathic symptoms during the study period were determined by examining Read codes for diabetic peripheral neuropathy screening and diabetic foot examination/screen (Table S3). The number/percentage of patients diagnosed with DPNP after neuropathic screening during the study period was calculated.

Analysis

To replicate the methodology of Hall et al,[12] the incidence rate of DPNP per 100,000 person-years of observation was calculated for the total study period and for the three 3-year subperiods: (1) July 1, 2002–June 30, 2005; (2) July 1, 2005–June 30, 2008; and (3) July 1, 2008–June 30, 2011. The incidence of DPNP was also estimated by sex and age groups (0–14, 15–29, 30–44, 45–59, 60–74, 75+ years).

The age group for each patient was determined using a reference year, which was either the start of the study period (2002 for the total study period as well as the first subperiod; 2005 for subperiod 2; and 2008 for subperiod 3), or the date of entry into the GPRD if this occurred later than the start of the study period. Confidence intervals (95% CI) for incidence rates were calculated based on Poisson exact CI. The incidence rates of DPNP for the three subperiods were compared using a Poisson regression model for each age group. The number of DPNP cases was the dependent variable, and the period indicator was included as an independent variable. Total years of observations were included as time of exposure. Results of patient characteristics, comorbidities, and medication are based on nonmissing data. All data analyses were carried out using SAS software version 9.2 (SAS Institute Inc., Cary, NC, USA).

Results

The total study population eligible for analysis was almost 7.5 million patients (Figure 1), providing approximately 38.1 million (38,118,838) person-years of observation. Of this total population, 50.9% were female, and the mean age was 35.3 years (standard deviation 23.5).

From the total study population, 6,779 patients were identified as having incident DPNP during the study period (Figure 1), and Table 1 summarizes the characteristics of this patient cohort.

Table 1 Characteristics of patient cohort with incident DPNP

Characteristic	n (%) or mean (SD)
Number of patients with incident DPNP during total study period	6,779
Sex, n (%)	
Female	3,083 (45.5)
Male	3,696 (54.5)
Age, mean (SD) years at DPNP incidence	65.5 (12.9)
Females	66.0 (13.5)
Males	65.0 (12.4)
Diabetes-related comorbidities*, n (%)	
Cardiovascular disease	453 (6.7)
Cerebrovascular and peripheral vascular disease	595 (8.8)
Retinopathy	484 (7.1)
Pain-related comorbidities*, n (%)	
Lower back pain	431 (6.4)
Osteoarthritis	362 (5.3)
CCI score, mean (SD)	0.97 (1.01)

Notes: *Comorbidities occurring in >5% of patients in the 12 months prior to diagnosis of DPNP. Other diabetes-related comorbidities examined included hypoglycemic events, other metabolic diseases, skin problems, nephropathy, obesity and anxiety. Other pain-related comorbidities examined included fibromyalgia syndrome, migraine, psoriatic arthropathy, and rheumatoid arthritis.
Abbreviations: DPNP, diabetic peripheral neuropathic pain; SD, standard deviation; CCI score, Charlson Comorbidity Index score; n, number.

The overall incidence of newly diagnosed DPNP during the whole study period was 17.8 per 100,000 person-years (95% CI = 17.4–18.2). Table 2 shows that the incidence of DPNP increased with age among both men and women, but it did not change significantly over the three subperiods, except among women aged 60–74 years, where the incidence decreased in the period 2008–2011 compared with the two earlier periods ($P = 0.001$).

During the whole study period, 90,162 patients in the total study population underwent neuropathic screening. Of these patients, 3,152 (3.5%) had a diagnosis of DPNP after neuropathic screening (but were not necessarily an incident case); and 1,053 (1.2%) were identified with incident DPNP. Of the 6,779 patients in the study cohort with incident DPNP, 1,053 (15.5%) had prior neuropathic screening during the study period (n = 109 for subperiod 1, n = 388 for subperiod 2, and n = 556 for subperiod 3).

A treatment for DPNP was initiated for 5,767 (85.1%) of the patients with incident DPNP within 28 days of diagnosis, and Table 3 summarizes the initial pharmacological treatment prescribed for these patients. Over the total study period, the most common single first-line treatments were TCAs (27.2%), anticonvulsants (17.0%), and NSAIDs (14.9%), with combination therapy being prescribed as the initial treatment for 26.6% of patients. There was little change in first-line medication use across the three subperiods, except for a slight decrease in the use of opioids and NSAIDs, and a very small increase in the use of SNRIs (Table 3). The most common combinations prescribed within 28 days of first diagnosis during the total study period were NSAIDs plus opioids (10.3%); TCAs, plus NSAIDs (9.6%); and TCAs plus opioids (8.6%).

Discussion

In this study, the overall incidence rate of DPNP in the UK primary care population using the GPRD was 17.8 cases per 100,000 person-years over the 9-year study period from 2002–2011. This is consistent with the previously reported DPNP incident rate of 15.3 cases per 100,000 person-years for 1992–2002,[12] where the number of incident cases (per 100,000 person-years) increased over time from 12.9 for 1992–1994, to 14.4 for 1995–1997, to 19.0 for 1998–2001, to 27.2 for 2002–2005. In contrast to the previous studies by Hall et al,[12,13] we found little change over time in the incidence of DPNP; the number of incident cases per 100,000 person-years was stable over the three consecutive 3-year periods (17.9, 17.2, and 18.4, respectively).

The total incident cases of DPNP (n = 6,779) during 2002–2011 out of 7.5 million primary care patients can be

Table 2 Incidence of DPNP per 100,000 person-years (95% CI) by sex, age group, and time period

	Subperiod 1 July 1, 2002–June 30, 2005	Subperiod 2 July 1, 2005–June 30, 2008	Subperiod 3 July 1, 2008–June 30, 2011
Total	17.9 (17.1–18.6)	17.2 (16.5–17.9)	18.4 (17.7–19.2)
Female			
0–14 years	–	–	–
15–29 years	0.6 (0.2–1.3)	0.9 (0.4–1.7)	1.2 (0.7–2.1)
30–44 years	6.4 (5.2–7.9)	5.1 (4.0–6.4)	5.3 (4.1–6.7)
45–59 years	20.4 (18.0–23.1)	19.1 (16.8–21.6)	20.5 (18.1–23.2)
60–74 years	48.7 (44.2–53.5)	47.9 (43.6–52.5)	38.7 (34.8–42.8)*
75+ years	48.6 (43.1–54.6)	41.2 (36.2–46.7)	50.2 (44.5–56.4)
Male			
0–14 years	–	–	–
15–29 years	0.7 (0.3–1.3)	0.6 (0.2–1.3)	1.1 (0.6–1.9)
30–44 years	6.1 (4.9–7.5)	5.4 (4.3–6.7)	5.4 (4.2–6.8)
45–59 years	26.8 (24.0–29.7)	25.1 (22.5–27.9)	28.4 (25.5–31.5)
60–74 years	61.9 (56.6–67.5)	61.7 (56.6–67.1)	64.1 (58.9–69.5)
75+ years	69.9 (61.2–79.4)	67.1 (59.0–76.1)	76.3 (67.5–85.9)

Notes: Poisson exact CI (95%) are given in brackets. *$P = 0.001$ from Poisson regression for trend of incidence rates.
Abbreviations: DPNP, diabetic peripheral neuropathic pain; CI, confidence interval.

translated into a crude prevalence rate of 0.5% in the general population, based on the assumption that prevalence is approximately the product of disease incidence and average disease duration, using an assumed duration of DPNP of 5 years.[20] Although there is little information on the natural history of DPNP, it is generally believed that painful symptoms resolve or become less prominent over time while the neuropathy continues to progress.[21,22] As of 2011, a total of 2.9 million people in the UK have been diagnosed with diabetes, giving an average diabetes prevalence rate of 4.5%.[23] Using this diabetes prevalence rate – and assuming that DPNP occurs in 21.0% of people with diabetes based on recent data from >15,000 UK patients with diabetes[5] – would provide a DPNP prevalence rate of 0.9% in the general population. While the estimates from our study do not provide a definitive indication of DPNP prevalence rates in the UK, they suggest that DPNP is being underdiagnosed in UK primary care. The results of our study also indicate that general practitioners (GPs) are not prescribing first-line treatments for neuropathic pain as recommended by clinical guidelines,[14,24] suggesting that other factors are being taken into consideration when selecting treatment for DPNP.

In clinical practice, DPNP is diagnosed based on clinical signs and symptoms, such as the type of pain, time of pain occurrence, and abnormal sensations; therefore, an accurate diagnosis relies on the patient's description of pain.[22,25]

Table 3 Initial treatment prescribed for incident DPNP by type of medication and study period

Medication	Subperiod 1 July 1, 2002–June 30, 2005 (n = 1,871)		Subperiod 2 July 1, 2005–June 30, 2008 (n = 1,940)		Subperiod 3 July 1, 2008–June 30, 2011 (n = 1,956)		Total study period July 1, 2002–June 30, 2011 (n = 5,767)	
	n	%	n	%	n	%	n	%
Nonopioid analgesics	47	2.5	38	2.0	46	2.4	131	2.3
Opioid	192	10.3	170	8.8	142	7.3	504	8.7
NSAIDs	354	18.9	297	15.3	210	10.7	861	14.9
Anticonvulsants	266	14.2	366	18.9	350	17.9	982	17.0
TCAs	505	27.0	490	25.3	574	29.4	1,569	27.2
SSRIs	28	1.5	31	1.6	31	1.6	90	1.6
SNRIs*	1	0.1	5	0.3	78	4.0	84	1.5
Duloxetine	0	0	4	0.2	75	3.8	79	1.4
Other antidepressants	2	0.1	2	0.1	7	0.4	11	0.2
Combination therapy	476	25.4	541	27.9	518	26.5	1,535	26.6

Notes: Data presented are number and percentage of initial prescriptions by type of medication within 28 days of first diagnosis of DPNP for the total study period and each subperiod. *SNRIs consist of duloxetine and venlafaxine. Duloxetine is also listed separately as it is the only SNRI recommended for DPNP. Combination therapy is defined as more than one pharmacotherapy prescribed on the same day.
Abbreviations: DPNP, diabetic peripheral neuropathic pain; NSAIDs, nonsteroidal anti-inflammatory drugs; TCA, tricyclic antidepressant; SSRIs, selective serotonin reuptake inhibitors; SNRI, serotonin norepinephrine reuptake inhibitor; n, number.

However, patients often do not link pain to diabetes or find it difficult to describe the symptoms they are experiencing and, therefore, may not report their pain symptoms to the doctor.[2,6,22] This could be one reason for the underdiagnosis of DPNP in primary care, and highlights the need for physicians to gather information on pain by prompting patients for relevant information, potentially using a simple screening form.[26] The annual foot examination and/or test for neuropathy in patients with diabetes is an ideal opportunity to diagnose DPNP, and is part of the QOF scheme for GP practices in the UK, which provides a financial incentive to complete these assessments.[6] However, the annual foot screen does not include specific screening questions on pain; there is no financial incentive for providing any diagnosis (including that of DPNP) arising from the assessment. Unexpectedly, we found that only 15.5% of patients with incident DPNP had a previous diabetic peripheral neuropathy screen or foot examination recorded in GPRD. This raises questions about how accurately screening is recorded in GPRD and whether it fully captures the QOF annual screening program, although a recent survey conducted by Diabetes UK found that a quarter of patients with diabetes could not recall having had an annual foot screen.[27] Our finding that more than one-half of the incident DPNP cases with prior neuropathic screening occurred in the last subperiod (2008–2011) suggests that diagnosis of DPNP may be improving and that the QOF scheme (introduced in 2004) may be helping. However, as screening was checked for during the total study period (2002–2011), patients identified with DPNP in subperiod 3 had a longer time for screening to be recorded than the patients in subperiod 1. Nevertheless, rates of screening are low and further research over the next few years should make this clearer.

There was a low frequency (<10%) of diabetes- and pain-related comorbidities in the 12 months before DPNP diagnosis, and the most common comorbidities were consistent with those reported previously in a retrospective database study of >11,000 patients with DPNP.[28] Some diabetes-related comorbidities (neuropathy, obesity, low levels of high-density lipoprotein cholesterol, and high levels of triglycerides) have been identified as independent risk factors for DPNP.[9]

In our study, the majority (85.1%) of patients with incident DPNP started pain-relief medication within 28 days. The most commonly used first-line medications were TCAs, anticonvulsants, and NSAIDs – despite a lack of evidence for NSAID efficacy in DPNP. SNRIs, such as duloxetine, were rarely prescribed as initial treatment. These findings are consistent with other studies in patients with DPNP.[3,9,12,20] Interestingly, treatment patterns at the time of first diagnosis of DPNP do not seem to have changed over the 9-year study period and, even in the last 3-year period (2008–2011), only 4.0% of patients received an SNRI as their initial medication. This indicates that patients are not being treated according to current clinical guidelines, which recommend duloxetine as first-line treatment for people with painful diabetic neuropathy, or amitriptyline, if duloxetine is contraindicated.[14] It is possible that patients are being prescribed TCAs (alone, or in combination with NSAIDs or opioids) because GPs are unsure of the diagnosis, and these antidepressants are known to be cheap and effective for the treatment of many painful conditions.

This study has several limitations. First, patients with incident DPNP were identified in the GPRD using multiple diagnostic codes covering diabetes, neuropathy, and neuropathic pain, together with prescription of pain relief medication. Although this was relatively straightforward and consistent with a previous publication,[12] more accurate data collection would be achieved if there was a consistent and clear definition of DPNP, and a diagnostic code that is uniformly used to record its presence. Second, because of the inclusion criteria, patients with diabetic neuropathy or diabetes plus neuralgia and taking medication for depression or another painful condition may be included, resulting in an overestimation of the incidence of DPNP. Third, our study cohort of patients with incident DPNP does not include patients with impaired glucose tolerance (prediabetes) that may have peripheral neuropathy and/or neuropathic pain.[29] Fourth, we were not able to assess pain severity in the GPRD, which may influence the diagnosis of DPNP and prescription of pain medication. Many patients with DPNP report having severe pain,[7] and those with severe pain are more likely to receive pain treatment.[10] Increasing pain severity is also associated with poorer patient outcomes and increased health care resource use and related costs.[30]

The strengths of our study include the large sample of primary care patients from the GPRD, which is representative of the UK population and utilizes real-life data that is routinely collected and recorded during primary care consultations. Importantly, as DPNP is typically diagnosed and managed in primary care, GPRD is the most appropriate data source available in the UK. Other strengths of this study are that we used similar methodology to Hall et al,[12] and the incidence of DPNP during the 9-year study period was well-defined.

Conclusion

In conclusion, our study provides up-to-date information on the incidence rate of DPNP in the UK primary care population. The incidence of DPNP increases with age and more

commonly affects men, but it has remained relatively stable over the past 9 years. However, our results suggest that DPNP is underdiagnosed in UK primary care and that treatment on diagnosis does not follow clinical guidelines, indicating the need for improved awareness and education about DPNP. If GPs can provide an early and confident diagnosis of DPNP, they may be more likely to implement treatments that reflect current clinical guideline recommendations, thereby improving patient care and reducing the burden of this disease.

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Disclosure

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Supplementary tables

Table S1 Read codes for diabetes

Medcode	Read code	Read term
1038	C100011	IDDM
15690	C103.00	DM with ketoacidotic coma
46963	C108000	IDDM with renal complications
57621	C108D00	IDDM with nephropathy
4513	C109.00	NIDDM
55842	C109200	NIDDM with neurological complications
17262	C109600	NIDDM with retinopathy
33343	C10y.00	DM with other specified manifestation
1682	C101.00	DM with ketoacidosis
53200	C101000	DM, juvenile type, with ketoacidosis
42505	C101z00	DM NOS with ketoacidosis
7795	C106.12	DM with neuropathy
59365	C109C00	NIDDM with nephropathy
63371	C10y100	DM, adult + other specified manifestation
13279	C104y00	Other specified DM with renal complications
56448	C108A00	IDDM without complication
9013	66AJ.11	Unstable diabetes
14889	C100111	Maturity onset diabetes
41389	C105100	DM, adult onset + ophthalmic manifestation
32556	C107.12	Diabetes with gangrene
1647	C108.00	IDDM
40401	C109500	NIDDM with gangrene
2471	K01x100	Nephrotic syndrome in DM
506	C100112	NIDDM
16491	C106.13	DM with polyneuropathy
67853	C106000	DM, juvenile + neurological manifestation
49276	C108100	IDDM with ophthalmic complications
26855	C108400	Unstable IDDM
6509	C108700	IDDM with retinopathy
52303	C109000	NIDDM with renal complications
62146	C109300	NIDDM with multiple complications
34912	C109400	NIDDM with ulcer
63762	C10z100	DM, adult onset + unspecified complication
64357	C10zz00	DM NOS with unspecified complication
50609	L180600	Preexisting DM, noninsulin-dependent
24490	C100000	DM, juvenile type, no mention of complications
52283	C108200	IDDM with neurological complications
29979	C109900	NIDDM without complication
40023	C102000	DM, juvenile type, with hyperosmolar coma
35105	C104100	DM, adult onset, with renal manifestation
35107	C104z00	DM with nephropathy NOS
32403	C107.11	DM with gangrene
17858	C108.12	Type 1 DM
52104	C108300	IDDM with multiple complications
6791	C108800	IDDM – poor control
66675	C10A000	Malnutrition-related DM with coma
31790	F372.00	Polyneuropathy in diabetes
22967	2BBF.00	Retinal abnormality – diabetes-related
711	C10.00	DM
14803	C100100	DM, adult onset, no mention of complications
35399	C107.00	DM with peripheral circulatory disorder
63357	C107100	DM, adult + peripheral circulatory disorder
18505	C108.11	IDDM
45467	C109B00	NIDDM with polyneuropathy
52236	C10A.00	Malnutrition-related DM
52212	Cyu2.00	[X] DM
34528	3882.00	Diabetes well-being questionnaire
50972	C100z00	DM NOS with no mention of complications
16502	C104.00	DM with renal manifestation
33807	C107200	DM, adult with gangrene
5884	C109.11	NIDDM
72320	C109A00	NIDDM with mononeuropathy
45491	C10z.00	DM with unspecified complication
17067	F171100	Autonomic neuropathy due to diabetes
55431	L180X00	Preexisting DM, unspecified
13069	66A8.00	Has seen dietitian – diabetes
54856	C101100	DM, adult onset, with ketoacidosis
21482	C102.00	DM with hyperosmolar coma
69748	C105000	DM, juvenile type + ophthalmic manifestation
34283	C105z00	DM NOS with ophthalmic manifestation
65025	C107z00	DM NOS with peripheral circulatory disorder
17859	C109.12	Type 2 DM
50429	C109100	NIDDM with ophthalmologic complications
38986	C100.00	DM with no mention of complications
43139	C102100	DM, adult onset, with hyperosmolar coma
72345	C102z00	DM NOS with hyperosmolar coma
68843	C103100	DM, adult onset, with ketoacidotic coma
33254	C105.00	DM with ophthalmic manifestation
16230	C106.00	DM with neurological manifestation
39317	C106100	DM, adult onset + neurological manifestation
44443	C108500	IDDM with ulcer
60499	C108600	IDDM with gangrene
31310	C108900	IDDM maturity onset
41716	C108C00	IDDM with polyneuropathy
8403	C109700	NIDDM, poor control
50960	L180500	Preexisting DM, insulin-dependent
24423	C108.13	Type 1 DM
18219	C109.13	Type 2 DM
24458	C109711	Type 2 DM, poor control
42729	C108E11	Type 1 DM with hypoglycemic coma
63017	C108911	Type 1 DM maturity onset
44440	C108E00	IDDM with hypoglycemic coma
62107	C109511	Type 2 DM with gangrene
55075	C109411	Type 2 DM with ulcer
62352	C108H11	Type 1 DM with arthropathy
42762	C109612	Type 2 DM with retinopathy
44779	C109E12	Type 2 DM with diabetic cataract
10642	ZC2C800	Dietary advice for DM
44260	C108F00	IDDM with diabetic cataract
46850	C108811	Type 1 DM, poor control
58604	C109611	Type 2 DM with retinopathy
47409	C109B11	Type 2 DM with polyneuropathy
17545	C108F11	Type 1 DM with diabetic cataract
64571	C109C11	Type 2 DM with nephropathy
65616	C108H00	IDDM with arthropathy
41049	C108712	Type 1 DM with retinopathy
66965	C109H12	Type 2 DM with neuropathic arthropathy
60699	C109F12	Type 2 DM with peripheral angiopathy

Table S1 (*Continued*)

Medcode	Read code	Read term
45914	C108812	Type 1 DM, poor control
56268	C109D11	Type 2 DM with hypoglycemic coma
50225	C109011	Type 2 DM with renal complications
18278	C109 J00	Insulin-treated Type 2 DM
48192	C109E11	Type 2 DM with diabetic cataract
24836	C109C12	Type 2 DM with nephropathy
37648	C109J11	Insulin-treated NIDDM
24693	C109G00	NIDDM with arthropathy
45919	C109212	Type 2 DM with neurological complications
66872	C108D11	Type 1 DM with nephropathy
70316	C109112	Type 2 DM with ophthalmic complications
60107	C108411	Unstable type 1 DM
45913	C109712	Type 2 DM, poor control
47816	C109H11	Type 2 DM with neuropathic arthropathy
18209	C109012	Type 2 DM with renal complications
61344	C108011	Type 1 DM with renal complications
65704	C109412	Type 2 DM with ulcer
43785	C109D00	NIDDM with hypoglycemic coma
18264	C109 J12	Insulin-treated Type 2 DM
51957	C108511	Type 1 DM with ulcer
38161	C108711	Type 1 DM with retinopathy
67905	C109211	Type 2 DM with neurological complications
61071	C109D12	Type 2 DM with hypoglycemic coma
18230	C108 J12	Type 1 DM with neuropathic arthropathy
49146	C108211	Type 1 DM with neurological complications
36633	C109K00	Hyperosmolar nonketotic state in type 2 DM
1549	C10E.00	Type 1 DM
758	C10F.00	Type 2 DM
12640	C10FC00	Type 2 DM with nephropathy
1407	C10FJ00	Insulin-treated Type 2 DM
18387	C10E700	Type 1 DM with retinopathy
21983	C108012	Type 1 DM with renal complications
69278	C109E00	NIDDM with diabetic cataract
18642	C10EH00	Type 1 DM with arthropathy
35385	C10FH00	Type 2 DM with neuropathic arthropathy
54899	C109F11	Type 2 DM with peripheral angiopathy
10418	C10ED00	Type 1 DM with nephropathy
25041	ZC2CA00	Dietary advice for type 2 diabetes
18496	C10F600	Type 2 DM with retinopathy
47954	C10F900	Type 2 DM without complication
32359	ZRbH.00	Perceived control of insulin-dependent diabetes
18390	C10FM00	Type 2 DM with persistent microalbuminuria
50813	C109A11	Type 2 DM with mononeuropathy
10692	C10EM00	Type 1 DM with ketoacidosis
39070	C10EE00	Type 1 DM with hypoglycemic coma
70766	C108E12	Type 1 DM with hypoglycemic coma
62674	C10FA00	Type 2 DM with mononeuropathy
47582	C10E000	Type 1 DM with renal complications
40837	C10EN00	Type 1 DM with ketoacidotic coma
32627	C10FN00	Type 2 DM with ketoacidosis
26054	C10FL00	Type 2 DM with persistent proteinuria
35288	C10E800	Type 1 DM, poor control
37806	C10FF00	Type 2 DM with peripheral angiopathy
40682	C10E900	Type 1 DM maturity onset

(*Continued*)

Table S1 (*Continued*)

Medcode	Read code	Read term
47649	C10E100	Type 1 DM with ophthalmic complications
34268	C10F200	Type 2 DM with neurological complications
44982	C10FE00	Type 2 DM with diabetic cataract
25627	C10F700	Type 2 DM, poor control
43921	C10E400	Unstable type 1 DM
49074	C10F400	Type 2 DM with ulcer
30294	C10EL00	Type 1 DM with persistent microalbuminuria
18777	C10F000	Type 2 DM with renal complications
12736	C10F500	Type 2 DM with gangrene
18683	C10E500	Type 1 DM with ulcer
36695	C10D.00	DM autosomal dominant type 2
46301	C10EC00	Type 1 DM with polyneuropathy
18425	C10FB00	Type 2 DM with polyneuropathy
61829	C108212	Type 1 DM with neurological complications
30323	C10EK00	Type 1 DM with persistent proteinuria
46624	C10C.11	Maturity onset diabetes in youth
54008	C10EJ00	Type 1 DM with neuropathic arthropathy
25591	C10FQ00	Type 2 DM with exudative maculopathy
51756	C10FP00	Type 2 DM with ketoacidotic coma
46917	C10FD00	Type 2 DM with hypoglycemic coma
22871	C10EP00	Type 1 DM with exudative maculopathy
62209	C10EM11	Type 1 DM with ketoacidosis
42831	C10E200	Type 1 DM with neurological complications
51697	C10G.00	Secondary pancreatic DM
47321	C10F100	Type 2 DM with ophthalmic complications
49949	C10E411	Unstable type 1 DM
49554	C10EF00	Type 1 DM with diabetic cataract
18143	C109G11	Type 2 DM with arthropathy
49869	C109G12	Type 2 DM with arthropathy
69043	ZC2C900	Dietary advice for type 1 diabetes
65267	C10F300	Type 2 DM with multiple complications
59253	C10FG00	Type 2 DM with arthropathy
51261	C10E.12	IDDM
69993	C10E600	Type 1 DM with gangrene
22884	C10F.11	Type 2 DM
60796	C10FL11	Type 2 DM with persistent proteinuria
47650	C10E300	Type 1 DM with multiple complications
59725	C109111	Type 2 DM with ophthalmic complications
12455	C10E.11	Type 1 DM
69676	C10EA00	Type 1 DM without complication
68105	C10EB00	Type 1 DM with mononeuropathy
64668	C10FJ11	Insulin-treated type 2 DM
55239	C10EQ00	Type 1 DM with gastroparesis
57278	C10F011	Type 2 DM with renal complications
49655	C10F611	Type 2 DM with retinopathy
63690	C10FR00	Type 2 DM with gastroparesis
47315	C10F711	Type 2 DM, poor control
54600	C10E412	Unstable IDDM
93468	C10EG00	Type 1 DM with peripheral angiopathy
53392	C10F911	Type 2 DM without complication
43227	C10F311	Type 2 DM with multiple complications
50527	C10FB11	Type 2 DM with polyneuropathy
45276	C10E312	IDDM with multiple complications
66145	C10EN11	Type 1 DM with ketoacidotic coma
72702	C10E812	IDDM, poor control
96506	C10G000	Secondary pancreatic DM without complication

(*Continued*)

Table S1 (*Continued*)

Medcode	Read code	Read term
66475	66Ak.00	Diabetic monitoring, lower risk albumin excretion
69163	8HTi.00	Referral to multidisciplinary diabetic clinic
62613	C10EA11	Type 1 DM without complication
57382	7272600	Laser photocoagulation to lesion of retina NEC
95813	9N1o.00	Seen in multidisciplinary diabetic clinic
61021	68AB.00	Diabetic digital retinopathy screening offered
72827	7P17100	Insulin secretion glucagon test
64142	8HI1.00	Referral for diabetic retinopathy screening
84142	44V6.00	Extended glucose tolerance test
91164	ZRB4.11	CSQ, Diabetes clinic satisfaction questionnaire
82474	8HI4.00	Referral to community diabetes specialist nurse
83532	66Ao.00	Diabetes type 2 review
83485	66Am.00	Insulin dose changed
85660	66An.00	Diabetes type 1 review
91646	C10F411	Type 2 DM with ulcer
91942	C10E311	Type 1 DM with multiple complications
91943	C10EC11	Type 1 DM with polyneuropathy
85336	7P17.00	Diagnostic endocrinology
90301	66Ag.00	Insulin needles changed daily
85991	C10FM11	Type 2 DM with persistent microalbuminuria
93380	C10N100	Cystic fibrosis-related DM
92979	7P17z00	Diagnostic endocrinology NOS
93390	9OLH.00	Attended DAFNE diabetes-structured education program
93491	9OLJ.00	DAFNE diabetes structured education program completed
93657	8Hj4.00	Referral to DESMOND diabetes structured education program
93631	9OLL.00	XPERT diabetes-structured education program completed
93704	8Hj3.00	Referral to DAFNE diabetes structured education program
93727	C10FE11	Type 2 DM with diabetic cataract
93854	9OLM.00	Diabetes-structured education program declined
93870	8Hj5.00	Referral to XPERT diabetes-structured education program
93875	C10E712	IDDM with retinopathy
93878	C10E511	Type 1 DM with ulcer

Abbreviations: IDDM, insulin dependent diabetes mellitus; CSQ, (Diabetes) clinic satisfaction questionnaire; DM, diabetes mellitus; NEC, not elsewhere classified; NOS, not otherwise specified; NIDDM, noninsulin dependent diabetes mellitus; DAFNE, Dose Adjustment For Normal Eating; DESMOND, Diabetes Education and Self-Management for Ongoing and Newly Diagnosed.

Table S2 Read codes for DPNP

Medcode	Read code	Read term
1. Painful diabetic neuropathy		
48078	F372000	Acute painful diabetic neuropathy
35785	F372100	Chronic painful diabetic neuropathy
2. Diabetic neuropathy (+ pain medication)		
2342	F372.12	Diabetic neuropathy
5002	F372.11	Diabetic polyneuropathy
16230	C106.00	DM with neurological manifestation
16491	C106.13	DM with polyneuropathy
17247	F35z000	Diabetic mononeuritis NOS
18056	2G5C.00	Foot abnormality, diabetes-related
18230	C108J12	Type 1 DM with neuropathic arthropathy
22573	C106z00	DM NOS with neurological manifestation
24694	C108B00	IDDM with mononeuropathy
27921	2G51000	Foot abnormality, diabetes-related
31790	F372.00	Polyneuropathy in diabetes
41716	C108C00	IDDM with polyneuropathy
42831	C10E200	Type 1 DM with neurological complications
43227	C10F311	Type 2 DM with multiple complications
44033	F345000	Diabetic mononeuritis multiplex
45276	C10E312	IDDM with multiple complications
45467	C109B00	NIDDM with polyneuropathy
45919	C109212	Type 2 DM with neurological complications
47409	C109B11	Type 2 DM with polyneuropathy
47650	C10E300	Type 1 DM with multiple complications
34152	G73y000	Diabetic peripheral angiopathy
34268	C10F200	Type 2 DM with neurological complications
35385	C10FH00	Type 2 DM with neuropathic arthropathy
37315	F3y0.00	Diabetic mononeuropathy
39317	C106100	DM, adult onset + neurological manifestation
39809	C108J00	IDDM with neuropathic arthropathy
54899	C109F11	Type 2 DM with peripheral angiopathy
55842	C109200	NIDDM with neurological complications
60208	C108J11	Type 1 DM with neuropathic arthropathy
60699	C109F12	Type 2 DM with peripheral angiopathy
72320	C109A00	NIDDM with mononeuropathy
91942	C10E311	Type 1 DM with multiple complications
7795	C106.12	DM with neuropathy
11663	M271100	Neuropathic diabetic ulcer – foot
61523	C106y00	Other specified DM with neurological comps
61829	C108212	Type 1 DM with neurological complications
65267	C10F300	Type 2 DM with multiple complications
67853	C106000	DM, juvenile + neurological manifestation
67905	C109211	Type 2 DM with neurological complications
98616	C10F211	Type 2 DM with neurological complications
99231	C108B11	Type 1 DM with mononeuropathy
101735	C10E212	IDDM with neurological comps
49146	C108211	Type 1 DM with neurological complications
50813	C109A11	Type 2 DM with mononeuropathy

(*Continued*)

Table S2 (*Continued*)

Medcode	Read code	Read term
52283	C108200	IDDM with neurological comps
54212	C109F00	NIDDM with peripheral angiopathy
3. Neuropathic (pain + diabetes)		
35537	Fyu7C00	[X] Polyneuropathy, unspecified
2790	F367.00	Peripheral neuropathy
3958	F366.00	Polyneuropathy
97306	Fyu7200	[X] Other specified polyneuropathies
55076	Fyu7.00	[X] Polyneuropathies and other disorder of peripheral nervous system
24226	F37z.11	Polyneuropathy unspecified
4. Neuralgia (+ diabetes + pain medication)		
2284	N242000	Neuralgia unspecified
54992	N242.00	Neuralgia, neuritis, and radiculitis unspecified
23839	N242z00	Neuralgia, neuritis, or radiculitis NOS

Note: [X] Cross referenced to specific ICD-10 codes (other READ terms relate to ICD-9).

Abbreviations: DPNP, diabetic peripheral neuropathic pain; DM, diabetes mellitus; IDDM, insulin-dependent diabetes mellitus; NIDDM, noninsulin-dependent diabetes mellitus.

Table S3 Read codes for DPNP screening

Medcode	Read code	Read term
1. Painful diabetic neuropathy		
10977	66Ac.00	Diabetic peripheral neuropathy screening
12247	8I6G.00	Diabetic foot examination not indicated
22823	66Ab.00	Diabetic foot examination
95994	66Aq.00	Diabetic foot screen

Abbreviation: DPNP, diabetic peripheral neuropathic pain.