ORIGINAL RESEARCH

Can diabetic polyneuropathy and foot ulcers in patients with type 2 diabetes be accurately identified based on ICD-10 hospital diagnoses and drug prescriptions?

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Purpose: We examined whether diabetic polyneuropathy (DPN) and diabetic foot ulcers in type 2 diabetes can be accurately identified using International Classification of Diseases, 10th revision discharge diagnosis codes, surgery codes, and drug prescription codes.
Methods: We identified all type 2 diabetes patients in the Central Denmark region, 2009–2016, who had ≥1 primary/secondary diagnosis code of "diabetes with neurological complication" (E10.4-E14.4), "diabetic polyneuropathy" (G63.2), or "polyneuropathy, unspecified" (G62.9). Patients with potential painful DPN and non-painful DPN were identified based on prescription history for serotonin–norepinephrine reuptake inhibitors, tricyclic antidepressants, or gabapentinoids. Likewise, type 2 diabetes patients with potential foot ulcers were identified based on diagnosis or surgery codes. We used medical record review as the reference standard and calculated positive predictive values (PPVs).
Results: Of 53 randomly selected patients with potential painful DPN, 38 were classified as having DPN when validated against medical records; of these, 18 also had neuropathic pain, yielding a PPV of 72% (95% CI: 58–83%) for DPN and 34% (95% CI: 22–48%) for painful DPN. Likewise, among 54 randomly selected patients with potential non-painful DPN, 30 had DPN based on medical record data; of these, 27 had non-painful DPN, yielding PPVs of 56% (95% CI: 41–69%) and 50% (95% CI: 36–64%), respectively. Secondary E-chapter codes often denoted stroke or mononeuropathies, rather than DPN. Excluding secondary E-chapter codes from the algorithm increased the PPV for DPN to 78% (95% CI: 63–89%) for the painful DPN cohort and to 74% (95% CI: 56–87%) for the non-painful DPN cohort. Of 53 randomly selected patients with potential diabetic foot ulcer, only 18 diagnoses were confirmed; PPV=34% (95% CI: 22–48%).
Conclusion: G-chapter and primary E-chapter diagnosis codes can detect type 2 diabetes patients with hospital-diagnosed DPN, and may be useful in epidemiological research. In contrast, our diabetic foot ulcer algorithm did not perform well.
Keywords: positive predictive value, epidemiology, registries, diabetic polyneuropathy, diabetic foot ulcer, type 2 diabetes

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Introduction

Diabetic polyneuropathy (DPN) is a common and serious diabetes complication.[1] One-fifth of patients with DPN may develop debilitating neuropathic pain.[2] Moreover, patients with DPN may suffer from a number of complications including

diabetic foot ulcers, lower extremity amputations, and death.[1] The etiology and pathogenesis behind painful and non-painful DPN, especially in type 2 diabetes,[3] are still not fully understood, which hinders effective prevention and improved treatment of DPN.

There may be a great potential in using large medical registries and administrative databases to study risk and prognosis of DPN in type 2 diabetes, if diagnosis codes of DPN and its complications are valid. A high validity would be expected for codes of well-defined conditions like death and extremity amputations,[4–8] whereas this may not be true for DPN and diabetic foot ulcers. Only a few studies have examined the potential of using diagnosis or procedure codes to identify patients with documented painful and non-painful DPN or diabetic foot ulcer. In a US study, an algorithm for painful diabetic peripheral neuropathy consisting of International Classification of Diseases (ICD) version 9 diagnosis codes was developed and validated against medical records in a diabetes registry.[9] The authors reported a positive predictive value (PPV) of 79% of the final algorithm.[9] Another US study found a PPV >90% of the specific ICD-9 code for "polyneuropathy in diabetes" (357.2) when compared with medical records,[10] whereas a third US study validated 5 different ways to identify diabetic foot ulcers using ICD-9 diagnosis codes and Current Procedural Terminology procedure codes and found PPVs between 55% and 88%.[11] These results are all from the US exclusively and based on ICD-9 codes. To our knowledge, the potential of using ICD-10 codes together with drug prescription registries to identify patients with painful DPN, non-painful DPN, or diabetic foot ulcer has not previously been studied.

Therefore, we examined whether hospital-diagnosed DPN, including painful DPN and non-painful DPN, and diabetic foot ulcers in patients with type 2 diabetes can be accurately identified using diagnosis codes, surgery codes, and drug prescription codes in Danish registries.

Materials and methods
Design and setting
This cross-sectional validation study is based on data from Danish medical registries and was conducted in the Central Region of Denmark (N≈1.3 million inhabitants), one of the five Danish administrative regions. The Danish National Health Service provides universal tax-supported health care for the entire Danish population including free access to general practitioners and

hospitals in Denmark and partial reimbursement for prescribed drugs.[12] Since 1968, the Danish Civil Registration System has assigned a unique 10-digit civil personal registration number (the CPR-number) to all Danish residents at birth or immigration.[4] The CPR-number is used in all Danish Registries and allows accurate and unambiguous individual-level linkage across the registries.[4]

Health registries
We used ICD-10 codes to identify type 2 diabetes patients with hospital-diagnosed DPN and diabetic foot ulcers in the Danish National Patient Registry (DNPR).[13] The DNPR holds information on all admissions at non-psychiatric hospitals since 1977, on non-psychiatric hospital outpatient and emergency room visits since 1995 and on all psychiatric hospital contacts (inpatient, outpatient, and emergency room) since 1995. From 1994 onwards, all diagnoses have been coded according to the ICD-10, whereas since 1996 all surgery has been coded according to the Nordic Medico-Statistical Committee classification of surgical procedures.[13] We used the National Health Service Prescription Database (NHSPD) to obtain complete information on prescriptions on glucose-lowering drugs and neuropathic pain medications in our patients.[12] The NHSPD has recorded data on redemption of reimbursed prescriptions from outpatient pharmacies since 2004. The recorded data include the amount and type of drug prescribed according to the Anatomical Therapeutic Chemical (ATC) classification system, and the date on which the drug was dispensed.[12]

Identification of the type 2 diabetes population
We defined eligible type 2 diabetes patients as those who had at least one in- or outpatient hospital discharge code of "diabetes mellitus" E10-14, "diabetic retinopathy" H36.0, "diabetes mellitus in pregnancy" O24 (excluding "gestational diabetes mellitus" O24.4), or "diabetic polyneuropathy" G63.2 at any hospital in Denmark, or at least one prescription redemption of a glucose-lowering drug, ATC-codes A10 between January 1, 1994, and July 10, 2016, N=436,402. This algorithm has previously been validated; the PPV of diagnosis codes for identifying patients with diabetes is 97% and the sensitivity 64%, whereas the PPV of the glucose-lowering drug prescription codes is 95% and sensitivity 72%.[14] To avoid inclusion of

patients treated with metformin for polycystic ovary syndrome, we did not include females aged 20–39 treated with metformin monotherapy who did not have a diabetes discharge code. We included other diabetes codes than the type 2 diabetes codes (E11), because type 1 diabetes, type 2 diabetes and other types of diabetes cannot be completely differentiated based on diagnosis codes E10-14 alone.[15] In order to minimize misclassification of patients with other types of diabetes than type 2 diabetes, we excluded patients younger than 30 years at diabetes diagnosis treated with insulin monotherapy (Table 1 and Figure 1).

Identification of DPN
Any DPN population
From the population of type 2 diabetes patients, we identified those who had an in- or outpatient hospital diagnosis code that was indicative of DPN: the potential DPN population, N=35,490. Codes indicative of DPN were "polyneuropathy, unspecified" G62.9, "diabetic polyneuropathy" G63.2, or "diabetes with neurological complication" E10.4, E11.4, E12.4, E13.4, E14.4 (excluding among the latter patients who also had a diagnosis code of G73.0 "amyotrophy", G99.0 "autonomic neuropathy", or G59.0 "mononeuropathy"). We included both primary (first-listed, ie the primary cause for the hospital contact) and secondary diagnosis codes. Only patients with a DPN code given on the same date or later than a first type 2 diabetes registration (diagnosis or prescription) were included in the DPN population.

Painful DPN population
Next, we combined the DPN-algorithm with prescription data on medications used for the treatment of neuropathic pain in order to define an algorithm to identify patients with potential painful DPN: the painful DPN population, N=6,978. A patient was considered to have painful DPN if that patient had a minimum of one prescription redemption of an anti-epileptic medicine; N03AX09, N03AX12, N03AX16, N03AG01, N03F01, N03F02, or a serotonin–norepinephrine reuptake inhibitor (SNRI)/tricyclic antidepressant (TCA); N06AX16, N06AX21, N06AA02, N06AA04, N06AA09, N06AA10, N06AA21. Prescriptions had to be redeemed within 1 year prior to and a half year after a DPN diagnosis and patients had to have no registration of a relevant exclusion diagnosis in DNPR from 1994 onwards. Exclusion diagnoses were epilepsy (G40, G41) for those with anti-epileptic medicine prescription redemption and depression/anxiety (F30-

Table 1 Algorithms of in- and outpatient discharge codes and prescription codes used to identify patients with painful and non-painful DPN and diabetic foot ulcer

Type 2 diabetes[a]
≥1 diabetes discharge code (E10-E14, H36.6, O24 [except O24.4], G63.2) OR ≥1 prescription of a glucose-lowering drug (ATC: A10)[b]
Potential DPN: Type 2 diabetes plus ≥1 discharge code for "diabetes with neurological complication" (E10.4, E11.4, E12.4, E13.4, E14.4)[c] OR Type 2 diabetes plus ≥1 discharge code for "diabetic polyneuropathy" (G63.2) OR Type 2 diabetes plus ≥1 discharge code for "polyneuropathy, unspecified" (G62.9)
Potential painful DPN: DPN plus ≥1 prescription code for antiepileptic drugs *minus* an epilepsy discharge code (G40+G41) OR DPN plus ≥1 prescription code for antidepressants (SNRI/TCA) *minus* a depression/anxiety discharge code (F30-F34, F40-42, F48.8 +F48.9)
Potential non-painful DPN: DPN patients that do not fulfil the criteria for painful DPN
Potential diabetic foot ulcer: Type 2 diabetes plus ≥1 discharge code for "diabetes with peripheral vascular complication" (E10.5, E11.5, E12.5, E13.5, E14.5) OR Type 2 diabetes plus ≥1 discharge code for "ulcer" (L97, L98.4, R02) OR Type 2 diabetes plus ≥1 discharge code for "osteomyelitis" (M86) OR Type 2 diabetes plus ≥1 surgery code for surgery of lower extremity (KQDA, KQDB, KQDG)

Notes: [a]All patients younger than 30 years at diagnosis treated with insulin monotherapy were excluded in order to minimize misclassification of type 1 diabetes patients. [b]Except females aged 20–39 prescribed metformin exclusively in order to minimize misclassification of patients with polycystic ovarian syndrome. [c]Excluding patients with ICD-10 codes for G73.0 amyotrophy, G99.0 autonomic neuropathy, G59.0 mononeuropathy.
Abbreviations: DPN, diabetic polyneuropathy; ICD-10, International Classification of Diseases; version 10; SNRI, serotonin–noradrenalin reuptake inhibitors; TCA, tricyclic antidepressants.

F34, F40-42, F48.8+F48.9) for those with SNRI/TCA prescription redemption. We did not include NSAIDs and opioids in our algorithm since these drugs are prescribed for a wider and more unspecific range of diseases and conditions.

Non-painful DPN population
DPN-patients who did not fulfill the criteria for painful DPN were considered to have potential non-painful DPN,
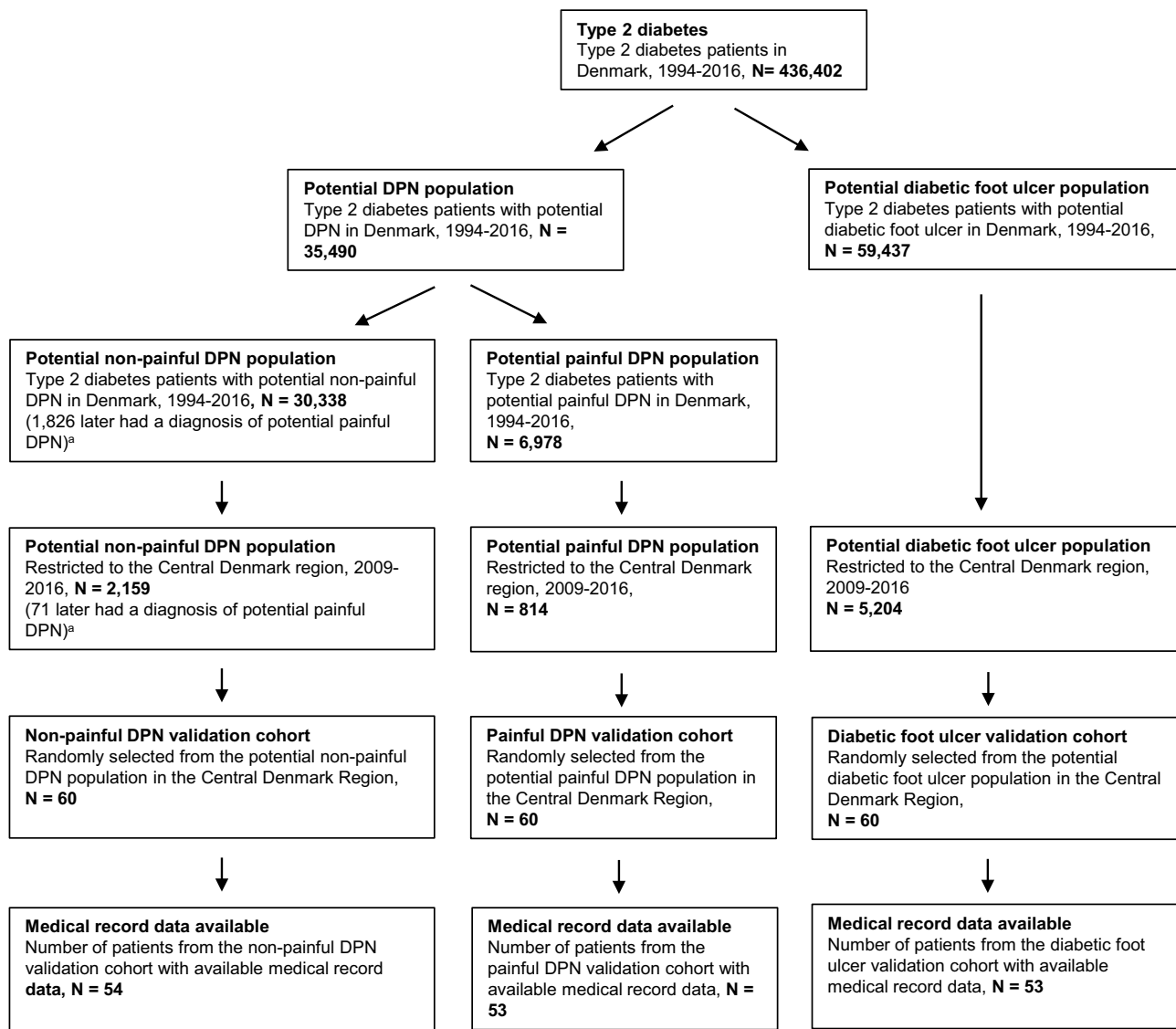
Figure 1 Flowchart of study population. Overview of patient selection. [a]Of the 30,338 patients with potential non-painful DPN, 1826 later fulfilled the criteria for potential painful DPN. Thus, these patients are included in both the non-painful and painful DPN populations at two distinct time points. Likewise, after restricting to the Central Denmark region, 2009–2016.
Abbreviation: DPN, diabetic polyneuropathy.

N=30,338. Of these, 1.826 patients fulfilled the criteria for non-painful DPN and at a later point of time fulfilled the criteria for painful DPN. Thus, they were included in both the non-painful DPN and the painful DPN population with two distinct DPN hospital contacts at two distinct time points.

Diabetic foot ulcer population

We identified all patients from the type 2 diabetes cohort who had at least one hospital diagnosis code or surgery code that was suggestive of diabetic foot ulcer. We used the following codes: "diabetes with peripheral vascular complication" E10.5-E14.5, "ulcer at lower extremity" L97, "chronic ulcer" L98.4, "gangrene" R02, "osteomyelitis" M86,

"treatment of ulcer at lower extremity" KQDB, "operations for chronic ulcer/fistula at lower extremity" KQDG, "puncture, incisions and local destructions of pathological tissue in the skin at the lower extremity" KQDA, N=59,437.

The painful DPN validation cohort, the non-painful DPN validation cohort, and the diabetic foot ulcer validation cohort

Next, we restricted the painful DPN population, the non-painful DPN population and the diabetic foot ulcer population to those with a diagnosis in the Central Denmark Region between January 1, 2009 and July 10, 2016 (N=814,

N=2,159, and N=5,204, respectively). Patients who had been seen at any department of neurology/neurophysiology, mixed internal medicine, endocrinology, dermatology, vascular surgery, plastic surgery, or orthopedic surgery, at one university hospital and four regional hospitals were randomly listed in each population (not taking into account age, gender, calendar year, specific diagnosis code, etc.) and the 60 first-listed individuals in each population constituted the painful DPN validation cohort, the non-painful DPN validation cohort, and the diabetic foot ulcer validation cohort, respectively.

Medical chart review

We attained permission to access medical record data on the 180 randomly selected patients from the Danish Health and Medicine Authorities. One physician (DHC) performed the medical record reviews. All cases with an uncertain diagnosis based on the available information were discussed with a specialist physician in diabetology (STK) and diagnoses were made according to consensus among the reviewing and specialist physician. We used a predefined checklist of symptoms, signs, and diagnostic test results described in the medical record as the gold standard (see Table 2 for details). We categorized patients from the painful DPN and non-painful DPN validation cohorts as "having DPN" if they fulfilled one of the following four criteria: 1) positive nerve conduction test supporting DPN; 2) ≥one symptom of polyneuropathy in feet (including neuropathic pain), eg numbness, prickling/tingling, shooting pain, stabbing pain; 3) ≥one sign of polyneuropathy, eg abnormal vibration, abnormal light touch, abnormal pinprick; or 4) physician notes documenting presence of polyneuropathy (eg noted in the medical record: "This T2D patient who has late complications including polyneuropathy, nephropathy…"). Patients, who did not fulfill one of these criteria, were categorized as "not having DPN". Moreover, if a patient had another more likely and significant cause of polyneuropathy (eg cancer, chemotherapy treatment, sarcoidosis, hereditary, and inflammatory polyneuropathy) the patient was also classified as "not having DPN". For alcohol overuse and vitamin B12 deficiency, severity and duration were often vaguely described,[16] and the diagnosis given by the treating physician was most often DPN despite alcohol overuse/B12 deficiency description in the medical records. Thus, only if it was unequivocally stated in the medical record that polyneuropathy was caused by these conditions, the patient was categorized as "not having

Table 2 Descriptions of symptoms and signs in both feet, and diagnostic test results used to verify DPN in the medical records

Use of the following descriptions/terms of symptoms and signs in both feet and test results in the medical record were used to verify DPN
Numbness
Prickling/tingling
Paresthesia
Hypoesthesia
Hypalgesia
Hyperalgesia/allodynia
Dysesthesia
Self-reported insensitivity or decreased sensitivity (eg "the patient reports decreased sensitivity in her feet")
Self-reported description of inability to differentiate between warm/cold
Abnormal prick-sensation/abnormal pinprick
Abnormal temperature
Abnormal vibration
Abnormal light touch
Abnormal position
Physician described "decreased sensitivity"
Positive nerve conduction test (by physician interpretation/ conclusion)
Physician documented diabetic polyneuropathy (eg "T2D patient with known complications including diabetic polyneuropathy, retinopathy.")
Neuropathic pain (described below)
Neuropathic pain – use of the following descriptions for pain in both feet the medical record were used to verify painful DPN
Burning pain
Pins/needles or stabbing pain
Shooting pain
Squeezing pain
Prickling/tingling described painful
Other neuropathic pain (to capture less frequents used descriptions/terms)
Hyperalgesia/allodynia

Abbreviation: DPN, diabetic polyneuropathy.

DPN". For all patients, it was noted whether neuropathic pain was described in the medical record.

We classified patients with explicitly noted "diabetic foot ulcer" in the medical record or with ≥one ulcer on toes/feet and no other pathogenesis to foot ulcer than diabetes (eg, trauma, gout) as "having diabetic foot ulcer". All other patients in the diabetic foot ulcer validation cohort were categorized as "not having diabetic foot ulcer".

Statistical analyses

Our study outcome was the PPV of the three algorithms defined as the proportion of painful DPN, non-painful

DPN and diabetic foot ulcer patients identified by the algorithms, which could be classified as having the disease when validated against the medical records. We provide 95% CIs as the exact binomial CI. For the painful DPN algorithm, we calculated both the PPV for having DPN (painful or non-painful) and the PPV for having painful DPN. Likewise, for the non-painful DPN algorithm, we calculated a PPV for having DPN (painful or non-painful) and non-painful DPN.

We stratified the PPVs according to hospital type, department type, admission type, diagnosis type, and diagnosis/surgery code. Moreover, we investigated different combinations of the diagnosis codes, eg, we separately investigated the PPV of the ICD-10 G-codes and the E-codes.

Research ethics and informed consent

This study was approved by the Danish Data Protection Agency (record number KEA-2015-13 and KEA-2015-4). Permission to access information from medical records without individually informed patient consent was granted by the Danish Health and Medicine Authorities (record number 3-3013-1479/1 and 3-3013-1479/2) in accordance with Danish law. Since this study was non-experimental and used only existing registry data, additional ethical committee approval was not required.

Results
Descriptive data

We were able to retrieve medical record data for 53 of 60 (88%) patients in the painful DPN validation cohort, 54 of 60 (90%) patients in the non-painful DPN validation cohort, and 53 of 60 (88%) patients in the diabetic foot ulcer validation cohort. Table 3 shows characteristics of the included patients. In all three cohorts most patients were diagnosed in the hospital outpatient clinic setting (painful DPN: n=44 [83%], non-painful DPN: n=41 [76%], diabetic foot ulcer: n=37 [70%]) versus inpatient setting. For both DPN validation cohorts, most patients were diagnosed in the departments of neurophysiology (painful DPN: n=22 [42%], non-painful DPN: n=18 [33%]), neurology (painful DPN: n=9 [17%], non-painful DPN: n=15 [28%]), or internal medicine (painful DPN: n=13 [25%], non-painful DPN: n=12 [22%]). In the diabetic foot ulcer validation cohort, 49% (n=26) had diagnosis codes only, 34% (n=18) had surgery codes only, and 17% (n=9) had both. The most frequent surgery

code was "treatment of ulcer at lower extremity" KQDB accounting for 86% (n=24) of all surgery codes (45% of patients in the diabetic foot ulcer validation cohort), whereas "diabetes with peripheral vascular complication" E10.5-E14.5 were the most used diagnosis codes accounting for 72% (n=26) of all diagnosis codes (49% of patients in the diabetic foot ulcer validation cohort). Most patients in the diabetic foot ulcer validation cohort were diagnosed in the departments of orthopaedic surgery (n=21 [40%]), vascular surgery (n=14 [26%]), or internal medicine (n=12 [23%]).

Positive predictive values

Of the 53 patients with potential painful DPN, 38 were classified as having DPN when validated against medical record data; of these, 19 had neuropathic pain, corresponding to a PPV of 72% (95% CI: 58–83) for hospital-diagnosed DPN and 36% (95% CI: 23–50) for painful DPN (Table 4). Among the 54 patients with potential non-painful DPN, 30 had DPN when validated against the medical records; of these, 27 had non-painful DPN, corresponding to PPVs of 56% (95% CI: 41–69) for hospital-diagnosed DPN and 50% (95% CI: 36–64) for non-painful DPN, respectively. E-chapter codes, especially when listed as a secondary diagnosis (Tables S1 and S2), were often used for other neurological conditions than DPN, such as stroke and mononeuropathies, in particularly at neurological departments. Restricting the algorithm to primary and secondary G-chapter codes and primary E-chapter codes yielded a PPV of 78% (95% CI: 63–89) for DPN and 40% (95% CI: 24–54) for painful DPN in the painful DPN validation cohort (N=45) and a PPV of 74% (95% CI: 56–87) for DPN and 65% (95% CI: 46–80) for non-painful DPN in the non-painful DPN validation cohort (N=34) (Table 4). Further restricting the algorithm to only G-chapter codes increased the PPV for DPN to 86% (95% CI: 70–95) and the PPV for painful DPN to 43% (95% CI: 26–61) among those with potential painful DPN (N=35). Among those with potential non-painful DPN (N=24), the PPVs for DPN remained unchanged (DPN: PPV =71% [95% CI: 49–87], non-painful DPN: PPV 67% [96% CI: 45–85]).

Among the 53 patients with potential diabetic foot ulcer, only 18 patients had diabetic foot ulcer based on the medical record data corresponding to a PPV of 34% (95% CI: 22–48). The PPVs for E10.5-E14.5 (N=26) and KQDB (N = 24), that constituted the most frequent diagnosis and surgery codes in the diabetic foot ulcer

Table 3 Descriptive data of hospital contacts of potential painful and non-painful DPN and potential diabetic foot ulcer identified using ICD-10 hospital codes and/or surgery in the DNPR and prescription codes in the NHSPD from 2009 to 2016

	Painful DPN, N=53	Non-painful DPN, N=54	Diabetic foot ulcer, N=53
Sex			
Male	34 (64)	40 (74)	34 (64)
Female	19 (36)	14 (26)	19 (36)
Age, years			
Median (quartiles)	64 (53–69)	67 (61–74)	74 (62–83)
Hospital type			
University hospital	22 (42)	20 (37)	19 (36)
Regional hospital	31 (58)	34 (63)	34 (64)
Department type			
Internal medicine	13 (25)	12 (22)	12 (23)
Neurological	9 (17)	15 (28)	1 (2)
Neurophysiological	22 (42)	18 (33)	0 (0)
Orthopaedic surgery	5 (9)	5 (9)	21 (40)
Vascular surgery	5 (8)	4 (7)	14 (26)
Dermatological	0 (0)	0 (0)	4 (8)
Plastic surgery	0 (0)	0 (0)	1 (2)
Admission type			
Inpatient	9 (17)	13 (24)	16 (30)
Outpatient	44 (83)	41 (76)	37 (70)
Diabetic foot ulcer code type			
Diagnosis code, only	N/A	N/A	26 (49)
Surgery code, only	N/A	N/A	18 (34)
Diagnosis+surgery code	N/A	N/A	9 (17)
Diagnosis code type[a]			
Primary diagnosis code	38 (72)	28 (52)	16 (30)
Secondary diagnosis code	16 (30)	26 (48)	19 (36)
Polyneuropathy – diagnosis code[b]			
E10.4-E14.4 (diabetes with neurological complication)	19 (36)	30 (56)	N/A
E10.4	2 (4)	8 (15)	N/A
E11.4	11 (21)	15 (28)	N/A
E12.4	0 (0)	0 (0)	N/A
E13.4	2 (4)	2 (4)	N/A
E14.4	4 (8)	5 (9)	N/A
DG62.9 (polyneuropathy, unspecified)	24 (45)	19 (35)	N/A
DG63.2 (diabetic polyneuropathy)	11 (21)	5 (9)	N/A
Type of neuropathic analgesics[c]			
Antiepileptic medicine			
Gabapentin	21 (40)	0 (0)	N/A
Pregabalin	14 (26)	0 (0)	N/A
Lamotrigine	2 (4)	0 (0)	N/A
Valproic acid	1 (2)	0 (0)	N/A
Carbamazepine	2 (4)	0 (0)	N/A
Oxcarbazepine	0 (0)	0 (0)	N/A

(*Continued*)

Table 3 (Continued).

	Painful DPN, N=53	Non-painful DPN, N=54	Diabetic foot ulcer, N=53
Serotonin–noradrenalin reuptake inhibitors			
Venlafaxine	1 (2)	0 (0)	N/A
Duloxetine	0 (0)	0 (0)	N/A
Tricyclic antidepressants		0 (0)	N/A
Imipramine	2 (4)	0 (0)	N/A
Clomipramine	0 (0)	0 (0)	N/A
Amitriptyline	23 (43)	0 (0)	N/A
Nortriptyline	6 (11)	0 (0)	N/A
Maprotiline	1 (2)	0 (0)	N/A
Diabetic foot ulcer – diagnosis and surgery codes[d]			
E10.5-E14.5 (DM with peripheral vascular complication)	N/A	N/A	26 (49)
L97 (ulcer of lower limb)	N/A	N/A	4 (8)
L98.4 (chronic skin ulcer, non specified)	N/A	N/A	5 (9)
R02 (gangrene)	N/A	N/A	0 (0)
M86 (osteomyelitis)	N/A	N/A	1 (2)
KQDA (puncture, incisions and local destructions of pathological tissue in the skin at the lower extremity)	N/A	N/A	2 (4)
KQDB (treatment of ulcer at lower extremity)	N/A	N/A	24 (45)
KQDG (operations for chronic ulcer/fistula at lower extremity)	N/A	N/A	2 (4)

Notes: [a]One patient was discharged with an A- and a B-diagnosis that were both included in the polyneuropathy algorithm. Thus the percentage does not sum up to 100%. [b]One patient was discharged with 2 different codes, that were both included in the in polyneuropathy algorithm. [c]39 patients had redeemed prescriptions of one type of ATC-code, 10 patients had redeemed prescriptions of two types of ATC-codes, 3 patents had redeemed prescriptions of three types of ATC-codes and 1 had redeemed prescriptions of five different types of ATC-codes. [d]Each patient may have been given one or more diagnosis codes and/or one or more surgery codes on the diabetic foot ulcer date.
Abbreviations: DPN; Diabetic polyneuropathy, ICD-10; International classification of diseases, version 10, DNPR; Danish National Patient Register, DHSPR; Danish Health Service Prescription Register, N/A; Not applicable, e.g. diabetic foot ulcer-defining codes not relevant for polyneuropathy groups and neuropathic pain treatment codes and polyneuropathy-defining codes not relevant for diabetic foot ulcer group.

validation cohort were 46% (95% CI: 27–67) and 29% (95% CI: 13–51) (Table S3). Around half of the E10.5-E14.5 codes represented peripheral ischemia rather than ulcer, and the remaining a mixture of conditions like Charcot foot, callosities, and clavus. The KQDB procedure code was often used for ulcers above malleoli level, ulcers in relation to gout, and debridement of callosities.

Discussion

The main finding of this study was that ICD-10 diagnosis codes for "diabetic polyneuropathy" G63.2, "polyneuropathy, unspecified" G62.9, and primary diagnosis codes for "diabetes with neurological complication" E10.4-E14.4 can be used to identify type 2 diabetes patients with hospital-diagnosed DPN in health care registers, whereas the secondary E-chapter codes often represented diseases like stroke or mononeuropathies. Patients with painful versus non-painful DPN could not be accurately distinguished based on prescription redemption of neuropathic pain treatment when validated against medical records. Finally,

our algorithm for diabetic foot ulcer did not perform well for identification of diabetic foot ulcer patients.

Validated against medical record data, Hartsfield et al[9] reported a PPV of 79% of an ICD-9 diagnosis code-based algorithm to identify patients with painful diabetic peripheral neuropathy (including other types of peripheral neuropathy, eg, mononeuropathies, autonomic peripheral neuropathy). In their initial algorithm, they found – like us – that prescription codes for neuropathic pain treatment did not perform well in identifying patients with painful diabetic neuropathy. There are several explanations for our low PPV for the presence of pain. First, even if a person has true neuropathic pain this may not necessarily be described in the medical record if the main reason for the hospital contact is unrelated to polyneuropathy, thus falsely underestimating the PPV for painful DPN. Second, we did not have data on possibly milder cases of treated depression/anxiety diagnosed by general practitioners. However, half of the painful DPN validation cohort patients with verified DPN and missing pain description

Table 4 Numbers and positive predictive values of potential DPN and diabetic foot ulcer

	Potential painful DPN, N=53					Potential non-painful DPN, N=54					Potential diabetic foot ulcer, N=53		
	Medical record review, conclusion			PPV (95% CI)		Medical record review, conclusion			PPV (95% CI)		Medical record review, conclusion		PPV (95% CI)
	Non-painful DPN	Painful DPN	Not DPN[a]	DPN	Painful DPN	Non-painful DPN	Painful DPN	Not DPN[a]	DPN	Non-painful DPN	Diabetic foot ulcer	Not diabetic foot ulcer	
Total	19	19	15	72 (58–83)	36 (23–50)	27	3	24	56 (41–69)	50 (36–64)	18	35	34 (22–48)
All G-codes and primary E-codes[b]	17	18	10	78 (63–89)	40 (24–54)	22	3	9	74 (56–87)	65 (47–80)	-	-	-
All G-codes	15	15	5	86 (70–95)	43 (26–61)	16	1	7	71 (49–87)	67 (45–84)	-	-	-

Notes: [a]Either not polyneuropathy or polyneuropathy is likely caused by other diseases. [b]Secondary E-codes often denoted stroke or mononeuropathies.
Abbreviations: DPN, diabetic polyneuropathy; PPV, positive predictive value.

in the medical record data were prescribed gabapentinoids. These drugs are primarily used for either hospital specialist diagnosed epilepsy (which we excluded) or neuropathic pain, suggesting that it was missing descriptions of true pain that led to falsely low PPVs.

Hoffman et al[10] evaluated the validity of different polyneuropathy codes among a general population and reported a PPV for DPN of 91% for the ICD-9 code "polyneuropathy in diabetes" 357.2 (N=105), which is similar to our result for the ICD-10 code "diabetic polyneuropathy" G63.2 (Table S1). The most frequently inaccurate coding was idiopathic polyneuropathy; 9% of validated patients coded with idiopathic polyneuropathy had diabetic polyneuropathy according to medical chart data. Likewise, another American study[17] found that diagnosis codes for idiopathic polyneuropathy were frequently used in patients with diabetic polyneuropathy. We did not include codes for idiopathic polyneuropathy in our algorithm. However, these codes were infrequently used in type 2 diabetes patients (including the codes would result in only 71 additional DPN patients, 0.2% of our total potential DPN population).

Sohn et al[11] evaluated one newly developed and four previously used diabetic foot ulcer algorithms against medical records. These algorithms varied in complexity. The algorithm most similar to ours – the Holzer algorithm defining diabetic foot ulcer by the use of at least one diagnosis or one procedure code – had a PPV of 72%, compared to our 34%. The remaining four algorithms had PPVs of 61–82%. Opposite to the algorithms validated by Sohn et al we included the frequently used "DM with peripheral vascular complication" E10.5-E14.5 codes, which also cover "Diabetes with foot ulcer" E10.5B-E14.5B. However, these codes turned out to have a low predictive value for diabetic foot ulcer, and as they had been given to half of the diabetic foot ulcer validation cohort, they diminished the overall PPV of our algorithm. A PPV of 82–89% has been reported for the ICD-9 code "ulcer of lower limbs, except decubitus" 707.1x,[6,11] corresponding to the ICD-10 diagnosis code L97 in our algorithm (our PPV: 75%, N=4). The L97 code may be valid in Danish registers as well; however, this needs to be investigated in a larger study.

A number of limitations need to be considered when interpreting our results.

First, we used medical record data as the reference standard, which may falsely lower the PPV due to incomplete information as described above. On contrary,

our criteria for verifying polyneuropathy were less stringent than those suggested by the Toronto Consensus Panels on DPN implying a risk of overestimation of the PPV.[18] Also, determination of intraepidermal nerve fiber density for the diagnosis of small-fiber polyneuropathy is not part of the everyday clinical examination for polyneuropathy and thus was not included in our criteria used to verify DPN based on the medical record data. However, since neuropathic pain in feet was a DPN verifying criteria in our study, we were also able to verify the DPN diagnosis among patients with small-fiber polyneuropathy. Second, we evaluated only the PPV and no other measures of validity, eg, sensitivity, specificity, and negative predictive value. The importance of different validity measures depends on the study question. A high PPV is important when identifying patient cohorts for studies of the prognosis of a given disease. Moreover, the PPV is a good approximation for the specificity when disease-prevalence is low, and even with low sensitivity, a high specificity will lead to unmeasured relative risks,[19] eg, in studies of DPN-risk factors. On contrary, low sensitivity may compromise studies of incidence and surveillance. Since we did not examine the sensitivity, cautious interpretation of DPN incidence and surveillance in studies based on the evaluated codes is necessary. Third, the study was conducted only in the Central Denmark region. However, the Danish health care system is uniform in its structure and practice; thus, our results are most likely generalizable to other parts of our country and countries with similar structure. Fourth, only a single reviewer evaluated most of the medical record data, and reviewers were not blinded to the registered discharge diagnosis codes, since a DPN- or diabetic foot ulcer-indicative diagnosis per definition had been given to all evaluated patients. Moreover, if discharge summaries or surgery descriptions were available (with the specific discharge diagnosis codes listed) they were included in the reviewed data. Finally, our validation sample sizes were small and a compromise between expected statistical power and practical feasibility, because we depended on health professionals at all involved departments to identify medical records for our study.

Conclusion

Our data suggest that G-chapter and primary E-chapter discharge diagnosis codes can detect patients with hospital-diagnosed DPN, and thus may be useful in epidemiological research. Our algorithm for diabetic foot ulcer did not perform well in identifying persons with diabetic foot ulcer, and a larger validation study to determine ways of identifying diabetic foot ulcers in Danish registers is warranted.

Disclosure

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