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Pharmacological Treatment Patterns in Neuropathic Pain—Lessons from Swedish Administrative Registries

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Conflict of interest: Anders Gustavsson and Christina Ljungcrantz were at time of the preparation of this manuscript employed at i3 Innovus, a contract research organization, and acting as consultants to the pharmaceutical industry. Johan Björkman is and Annica Rhodin was at the time of this study employed at Grünenthal, a pharmaceutical company.

Abstract

Objective. To explore the treatment patterns of patients with a diagnosis related to chronic pain (DRCP) initiating pharmacological treatment indicated for neuropathic pain (NeuP: tricyclic antidepressants, serotonin–norepinephrine reuptake inhibitors, and anticonvulsants).

Design. Retrospective study on administrative registers.

Setting. General population in Western Sweden (one sixth of the country).

Subjects. All patients with a DRCP (N = 840,000) in years 2004–2009.

Outcome Measures. Treatment sequence, continuation, switching, and comedication.

Results. In total, 22,997 patients with a first NeuP in 2007 or 2008 were identified, out of which 2% also had epilepsy and 39% had a mood disorder. The remaining 13,749 patients were assumed to be treated for neuropathic pain, out of which 16% had a neuropathy diagnosis, 18% had a mixed pain diagnosis, and the remaining 66% had another DRCP. The most common first prescription was amitriptyline (40%) followed by pregabalin (22%) and gabapentin (19%). More than half had discontinued treatment after 3 months, and 60–70% at 6 months. Seven percent received another NeuP drug within 6 months of the discontinuation of their first NeuP treatment, 11% had another analgesic and 22% had a prescription indicating psychiatric comorbidity (selective serotonin reuptake inhibitors or benzodiazepine).

Conclusions. Treatment initiation of currently available drugs indicated for neuropathic pain less frequently lead to long-term treatment in clinical practice compared with clinical trial, and few try more than one drug. We suggest our findings to be indications of a need for better routines in diagnosing patients to ascertain optimal treatment and follow-up.

Key Words. Chronic Pain; Tricyclic Antidepressants; Serotonin–Norepinephrine Reuptake Inhibitors; Anticonvulsants; Treatment Pattern; Psychiatric Comorbidity

Introduction

Neuropathic pain is caused by somatosensory system disease or damage and thereby differs from nociceptive pain which may have different pathophysiology [1]. However, many pain syndromes may be caused by a combination of both [2], often referred to as mixed pain. Many chronic pain conditions may also include components where our knowledge about pathophysiology is even less clear, so far best categorized as

idiopathic pain. Neuropathic pain affects up to 7–8% of the general population [3] and is associated with substantially impaired quality of life of patients [4–8]. Between 17% and 51% of all patients with chronic pain also report neuropathic components of their pain, varying by study and methodology [9–11]. Patients with neuropathic components of pain have been reported to have more analgesic treatment and lower quality of life than comparative chronic pain patients [10,11]. Neuropathic pain is also commonly a long-term condition which is difficult to treat as the recommended pharmacological treatments often have insufficient symptomatic effects and in particular unacceptable side effects. In a study on patients with chronic painful diabetic neuropathy, about 75% reported pain of similar severity after 5 years [12].

The current international guidelines on pharmacological treatment of neuropathic pain recommend tricyclic antidepressants (TCA) (e.g., amitriptyline and nortriptyline), gabapentin and pregabalin as first line for most conditions [3]. Serotonin–norepinephrine reuptake inhibitors (SNRI) including duloxetine and venlafaxine are recommended for first-line treatment of painful diabetic polyneuropathy. Tramadol and strong opioids should be used as second and third line, respectively. Swedish guidelines from the Medical Products Agency are largely consistent with the international guidelines with certain exceptions including specifying TCA and gabapentin as first-line treatment in peripheral neuropathic pain [13].

In two recent studies, Swedish registry data were analyzed to describe the socioeconomic burden of patients with a diagnosis related to chronic pain [14], and the treatment patterns of patients initiating treatment with a slow release strong opioid (Gustavsson et al. [15] manuscript submitted). In this third manuscript, we study the treatment pattern of patients initiating treatment with a drug indicated for neuropathic pain. The available register data provide a unique opportunity to explore how these drugs are used in clinical practice.

The objectives of this study were to describe the characteristics and treatment patterns of patients initiating a drug treatment indicated for neuropathic pain, including which drugs were selected and in what sequence, discontinuation rates, and what comedications patients were prescribed.

Methods

Patients were identified in the Vega register maintained by a regional health authority in Western Sweden (Västra Götalandsregionen) with a total population of 1.56 million inhabitants. In total, 837,896 patients were selected having an inpatient or outpatient diagnosis related to chronic pain, as previously defined [14,16], at any point in time between January 1, 2004 and November 30, 2009. The prescription patterns of the selected patients were further extracted from the national prescriptions register held by the National Board of Health and Welfare (Socialstyrelsen). Data on prescriptions were available between July 1, 2005 and November 30, 2009.

The prescription patterns were explored of patients on: TCA (amitriptyline, clomipramine, nortriptyline), SNRI (duloxetine, venlafaxine), and anticonvulsants (gabapentin, pregabalin). For simplicity, we will refer to these treatments as NeuP treatments or prescriptions. Only patients getting their first prescription between January 1, 2007 and December 31, 2008 were considered in the analysis. That is, patients included were not allowed to have any prescription from July 1, 2005 to December 31, 2006. By this measure, we ascertained that this was their first NeuP prescription in at least 18 months. Patients may have received a prescription before July 2005. Furthermore, each patient could be followed at least 11 months, as the data were available throughout November 2009. Only patients with a single first NeuP treatment were included in the analysis.

Patients were stratified into three diagnosis groups (Table 1). First, we identified all patients with a neuropathy diagnosis. Second, we identified all patients with cervicalgia, sciatica, or lumbago with sciatica. These diagnoses were selected because we believe they represent patients that commonly have neuropathic combined with nociceptive and/or idiopathic components of pain. We will refer to this diagnosis group as mixed pain, although we acknowledge that there is no consensus on which diagnosis that should be considered of mixed etiology. The remaining patients had another diagnosis related to chronic pain as presented in an earlier study [14]. Patients with a diagnosis of epilepsy (International Classification of Disease tenth revision [ICD-10] G40-G41) and/or mood disorder (ICD-10 F30-F39) were excluded in order to reduce the risk of including patients that had received the same drugs for other indications than neuropathic pain.

The proportion of patients continuing treatment over time was explored using survival analysis methods. Patients were assumed to discontinue treatment if they did not refill the prescription within 6 months from the latest dispatch, but were censored when no more data were available. The date of discontinuation was assumed to be the date of the last dispatch plus the mean number of days between each two dispatches in the total sample. Switches to another NeuP prescription drug within 6 months of the last dispatch of the first NeuP treatment, delayed switches (>6 months after the last dispatch of the first NeuP treatment), and add-on NeuP prescriptions (another prescription in between two dispatches of the first NeuP drug) were explored. Finally, the proportion of patients on any prescribed pain treatment was explored, including the analgesics listed in Table 4.

Results

In total, 11,699 patients were identified with a first NeuP prescription in 2007 and 11,298 in 2008 (Table 2). These constituted about 3% of those identified with a diagnosis related to chronic pain, or 1.5% of the total underlying

Table 1 The diagnosis groups used to stratify patients with a presumed prescription for neuropathic pain

Group	Diagnoses (ICD-10)
Neuropathy	Trigeminal neuropathies (G50), Diseases of other cerebral nerves (G52), Cerebral neuropathies in diseases classified elsewhere (G53), Nerve root and plexus diseases (G54), Nerve root and plexus compression in diseases classified elsewhere (G55), Mononeuropathies of the upper extremity (G56), Mononeuropathies of the lower extremity (G57), Other mononeuropathies (G58), Mononeuropathy in diseases classified elsewhere (G59), Hereditary and idiopathic neuropathy (G60), Polyneuritis (G61), Other polyneuropathies (G62), Polyneuropathy in diseases classified elsewhere (G63), Other diseases of the peripheral nervous system (G64), Paraplegia and tetraplegia (G82), Postprocedural disorders of nervous system, not elsewhere classified (G97), Other disorders of bone (M89), Other symptoms and signs involving the nervous and musculoskeletal systems (R29)
Mixed pain	Cervicalgia (M54.2), Sciatica (M54.3), Lumbago with sciatica (M54.4)
Other diagnosis related to chronic pain (DRCP)	Cancer, Specific back conditions, Intervertebral disc disorder, Arthritis, Fractures, Multimorbidities, Headaches and Other conditions associated with chronic pain [14,15]

population in Western Sweden. About 2% (N = 472) of the identified patients with a prescription had an epilepsy diagnosis (ICD-10 G40-G41), and 39% (N = 8,988) had a mood disorder diagnosis (ICD-10 F30-F39) in their outpatient or inpatient records. These were excluded from the subsequent analysis, resulting in a total sample of 13,749 patients that were assumed to get their prescription for treatment of neuropathic pain (Table 2). Sixteen percent of these patients had a neuropathy diagnosis at some point in time, 18% had mixed pain, and the remaining 66% had other diagnoses related to chronic pain. The patients' age at the first prescription ranged between 6 and 102 years, and about two thirds of patients were female.

The most commonly prescribed first NeuP prescription was the TCA amitriptyline, followed by either of the anticonvulsants pregabalin or gabapentin (Table 2). The anticonvulsants were relatively more common in patients with a neuropathy or mixed pain diagnosis, especially gabapentin, whereas venlafaxine was more common in patients with other diagnoses related to chronic pain. A little more than half of all patients had a second dispatch, and the time to this second dispatch was 37 days on average.

Half of all patients had discontinued treatment over the first 47–160 days depending on the drug. Over the 3 years of observation, only 10–20% of patients remained on their

Table 2 Demographics and treatment patterns of patients on their first NeuP prescription stratified by diagnosis

	All	Neuropathy	Mixed pain	Other DRCP
Number of patients	13,749	2,220	2,498	9,031
Mean age (SD)	55.6 (18)	58.7 (19)	54 (16)	55.2 (17)
Number of males (%)	5,094 (37%)	864 (39%)	997 (40%)	3,233 (36%)
Discontinuation				
Number of patients with second dispatch within 6 months (%)	7,508 (55%)	1,215 (55%)	1,284 (51%)	5,009 (55%)
Mean days to second dispatch (SD)	37.1 (37)	37.3 (37)	38 (38)	36.9 (37)
Distribution across prescription drugs (% of all first prescriptions)				
Amitriptyline	5,531 (40%)	796 (36%)	972 (39%)	3,763 (42%)
Clomipramine	328 (2%)	31 (1%)	39 (2%)	258 (3%)
Nortriptyline	33 (0%)	8 (0%)	12 (0%)	13 (0%)
Duloxetine	1,108 (8%)	117 (5%)	145 (6%)	846 (9%)
Venlafaxine	1,051 (8%)	83 (4%)	86 (3%)	882 (10%)
Gabapentin	2,681 (19%)	635 (29%)	648 (26%)	1,398 (15%)
Pregabalin	3,017 (22%)	550 (25%)	596 (24%)	1,871 (21%)

DRCP = diagnosis related to chronic pain; NeuP = pharmacological treatment indicated for neuropathic pain; SD = standard deviation.

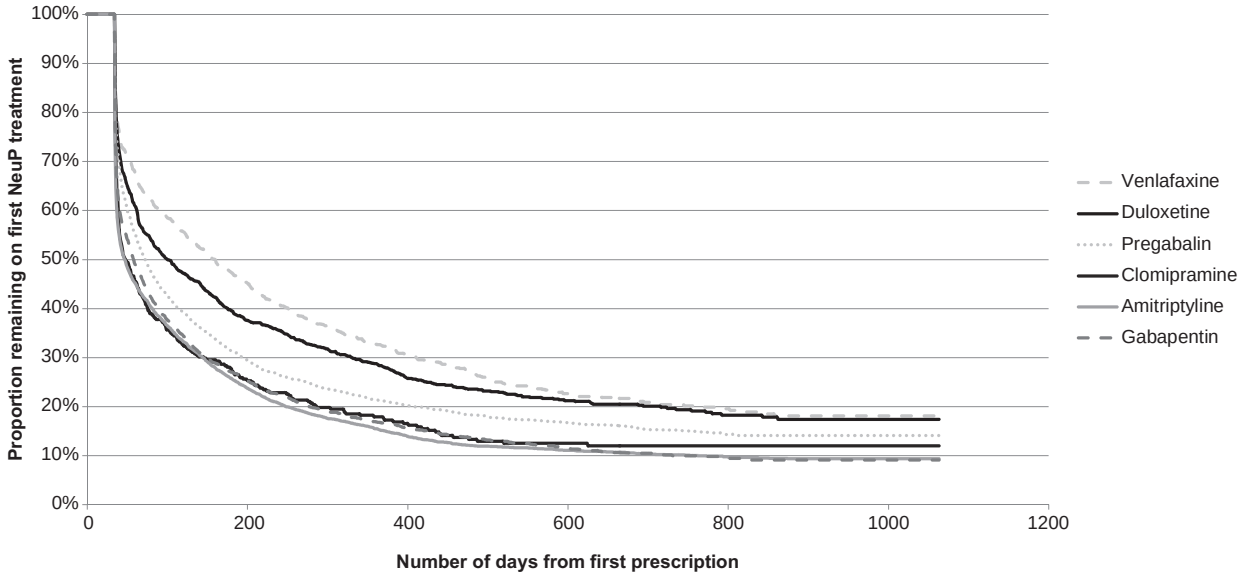

Figure 1 Proportion of patients on their first pharmacological treatment indicated for neuropathic pain (NeuP) over time, by treatment*.

* The Kaplan–Meier curves show the proportion continuing treatment over time out of all patients that are still under observation. In absence of any mortality data, patients were considered to be under observation until the end of the data capture (November 30, 2009). Patients were censored 182 days before the end of the data set as we could not ascertain that they would not have another dispatch within 6 months after this time. For instance, those initiating treatment on December 1, 2008 are only observed over 365 days as data were only available up until November 30, 2009. Furthermore, if they had another dispatch in April 2009 and another in August 2009, they were continuers until August and then considered to be censored (excluded from subsequent analysis) because we did not know if they continued after this time or not. We assumed that patients discontinue if there was no additional dispatch within 182 days from the last dispatch. They were assumed to discontinue 37 days after the last dispatch (mean duration of each dispatch). Only patients with single first prescriptions were included (i.e., patients with two NeuP prescriptions at the same date were excluded). Nortriptyline was excluded due to insufficient number of observations.

first NeuP treatment (Figure 1). Patients on gabapentin and amitriptyline tended to discontinue first whereas patients starting on venlafaxine or duloxetine continued a little longer.

We did not have any information of the cause of discontinuation, and we did not have any data on mortality. Instead, we explored the proportion of patients that remained on treatment out of those that were still in contact with health care. That is, patients were censored 6 months prior to their last record in the registers. This resulted in a somewhat higher proportion of patients remaining on treatment but still below 22% over 3 years (Figure 2).

The proportion of patients on any NeuP prescription differed slightly across the three diagnosis groups (Figure 3). Out of those that were still in contact with health care, patients with other diagnoses related to chronic pain continued with their treatment to the largest extent followed by those with a neuropathy diagnosis. Irrespective of diagnosis, half had discontinued within 3 months, about 60–70% had discontinued after 6 months, and less than 19% remained after 3 years.

About an eighth of all patients had a second NeuP drug (i.e., another TCA, SNRI, or anticonvulsant but different than the first drug) after their first NeuP prescription drug (Table 3). A little less than half of these (7%) were switching drugs within 6 months of the last dispatch of their first drug, whereas the remaining either had two prescriptions in parallel (add-on) or discontinued the first drug treatment and then only got another one until more than 6 months had past from the last dispatch of the first drug. Patients with a neuropathy diagnosis were more likely to get a second NeuP drug (24%). Pregabalin was the most common second NeuP drug followed by amitriptyline and gabapentin.

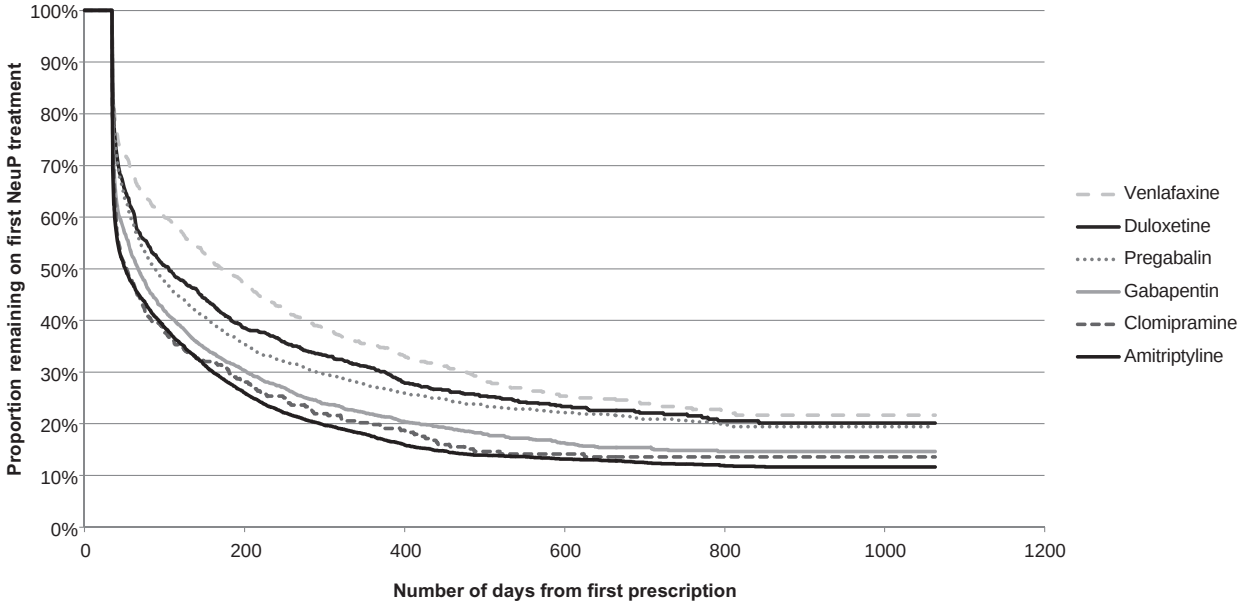

Figure 2 Proportion of patients on their first pharmacological treatment indicated for neuropathic pain (NeuP) over time (only considering those with a subsequent health care contact), by treatment*.
* In this graph, patients were considered to be under observation until their last individual record in the database (including drug prescription, outpatient care, inpatient care, decision on sick leave, or early retirement). That is, patients were censored if they did not have a health care contact within the next 6 months, from their last dispatch. Nortriptyline was excluded due to insufficient number of observations.

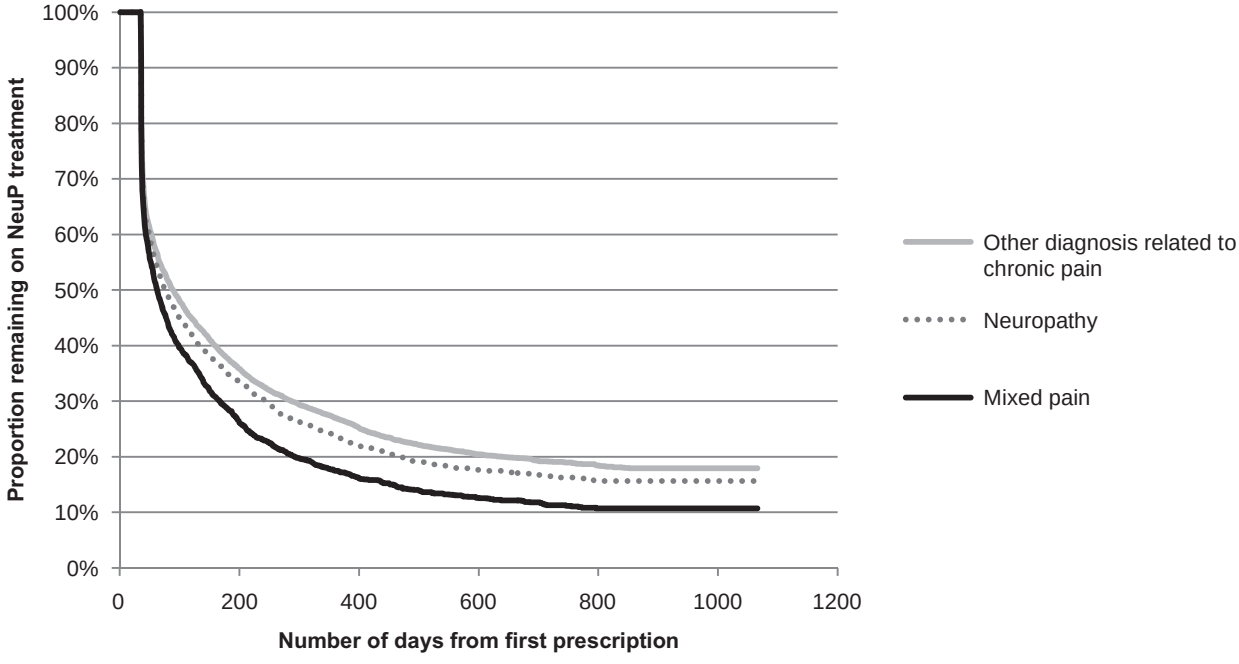

Figure 3 Proportion of patients on any pharmacological treatment indicated for neuropathic pain (NeuP) over time by diagnosis group (only considering those with a subsequent health care contact).

Table 3 Treatment patterns of patients on their second NeuP prescription stratified by diagnosis

	All	Neuropathy	Mixed pain	Other DRCP
Patients with second NeuP prescription drugs (% of all with first NeuP prescription)				
Total number of patients	2,250 (16%)	523 (24%)	452 (18%)	1,275 (14%)
Thereof switches	1,005 (7%)	236 (11%)	196 (8%)	573 (6%)
Thereof delayed switches*	745 (5.4%)	167 (7.5%)	179 (7%)	399 (4.4%)
Thereof add-ons**	500 (3.6%)	120 (5.4%)	77 (3%)	303 (3.4%)
Distribution across prescription drugs (% of all second NeuP prescription drugs)				
Amitriptyline	570 (25%)	148 (28%)	104 (23%)	318 (25%)
Clomipramine	54 (2%)	14 (3%)	9 (2%)	31 (2%)
Nortriptyline	29 (1%)	10 (2%)	6 (1%)	13 (1%)
Duloxetine	293 (13%)	44 (8%)	49 (11%)	200 (16%)
Venlafaxine	98 (4%)	5 (1%)	15 (3%)	78 (6%)
Gabapentin	452 (20%)	138 (26%)	97 (21%)	217 (17%)
Pregabalin	754 (34%)	164 (31%)	172 (38%)	418 (33%)

DRCP = diagnosis related to chronic pain; NeuP = pharmacological treatment indicated for neuropathic pain.
* More than 6 months after the last dispatch of the first NeuP treatment.
** Another prescription in between two dispatches of the first NeuP drug.

A small proportion of patients (11%) had an added analgesic prescription in parallel to their NeuP (Table 4). The most common drugs were strong (step III) opioids and nonsteroidal anti-inflammatory drugs, paracetamol, and acetylsalicylic acid. More than a fifth (22%) of patients were also prescribed a psychiatric drug (selective serotonin reuptake inhibitor [SSRI] or benzodiazepines).

Few (7%) of those discontinuing treatment with a NeuP switched or remained on another analgesic drug (Table 5). There were small differences across diagnosis groups, i.e., slightly more patients on treatment in the mixed pain group compared with the other two groups. Figure 4 shows the proportion of patients continuing on treatment out of those that were still in contact with health care. Less than 20% of patients that were still in contact with health care had any analgesic treatment 2 years after their first NeuP prescription.

Discussion

This study describes the patient population with a diagnosis related to chronic pain that initiates a treatment indicated for NeuP, and their pharmacological treatment pattern. It shows that, after removing patients with epilepsy and mood disorders, only a small proportion (16%) of those with a first NeuP prescription in 2007 or 2008 have a neuropathy diagnosis. A little more have what we have chosen to denote a mixed pain diagnosis (18%), while the majority have another diagnosis related to chronic pain (66%) such as cancer, specific back conditions, intervertebral disc disorder, arthritis, fractures, multimorbidities, and headaches [14]. The latter group includes indications for which TCA, SNRI, or anticonvulsants may also be indicated, e.g., headache for which amitriptyline has been shown to have an effect [17]. Still, a large proportion of patients in the other diagnosis group has probably been

Table 4 Number of patients with another analgesic prescription as add-on to their first NeuP treatment (proportion of all)

	All	Neuropathy	Mixed pain	Other DRCP
Any non-NeuP prescription	1,525 (11%)	225 (10%)	298 (12%)	1,002 (11%)
NSAIDs (including ASA and paracetamol)	1,233 (9%)	191 (9%)	240 (10%)	802 (9%)
Weak (step II) opioids	457 (3%)	75 (3%)	123 (5%)	259 (3%)
Strong (step III) opioids	1,382 (10%)	199 (9%)	258 (10%)	925 (10%)
Triptans	26 (0%)	1 (0%)	9 (0%)	16 (0%)
Any psychiatric comedication	2,964 (22%)	384 (17%)	379 (15%)	2,201 (24%)
SSRI	1,337 (10%)	179 (8%)	169 (7%)	989 (11%)
Benzodiazepines	1,846 (13%)	229 (10%)	248 (10%)	1,369 (15%)
Other sedatives i.e., hydroxyzine	538 (4%)	63 (3%)	57 (2%)	418 (5%)

ASA = acetylsalicylic acid; DRCP = diagnosis related to chronic pain; NeuP = pharmacological treatment indicated for neuropathic pain; NSAID = nonsteroidal anti-inflammatory drugs; SSRI = selective serotonin reuptake inhibitors.

Table 5 Number of patients with another analgesic prescription within 6 months after discontinuation of their last NeuP treatment (proportion of all discontinuers with a subsequent health care contact)

	All	Neuropathy	Mixed pain	Other DRCP
Any non-NeuP prescription	774 (7%)	131 (7%)	198 (9%)	445 (7%)
NSAIDs (including ASA and paracetamol)	677 (6%)	108 (6%)	176 (8%)	393 (6%)
Weak (step II) opioids	321 (3%)	46 (3%)	109 (5%)	166 (2%)
Strong (step III) opioids	448 (4%)	81 (5%)	95 (4%)	272 (4%)
Triptans	23 (0%)	2 (0%)	5 (0%)	16 (0%)

ASA = acetylsalicylic acid; DRCP = diagnosis related to chronic pain; NeuP = pharmacological treatment indicated for neuropathic pain; NSAID = nonsteroidal anti-inflammatory drugs.

prescribed one of these drugs because the treating physician wanted to target a neuropathic pain component. Some patients may have received their treatment ex juvantibus to test a neuropathic component of pain, but if so, they were never given a diagnosis at follow-up either. Thus, the large "rest group" of 66% indicates a problem of setting diagnosis in clinical practice. Only one third of the patients had received a precise diagnosis indicating the need for treatment of NeuP.

We excluded 39% of all patients with a first NeuP prescription because they had a mood disorder diagnosis. Still, 22% of the remaining patients were comedicated with an SSRI or benzodiazepine. This implies that 52% of all patients with a first NeuP prescription in 2007 or 2008 either had a mood disorder diagnosis or a comedication indicating a mood or anxiety disorder. The relatively large proportion that had these comedications but no mood disorder diagnosis likely includes a portion of patients that were never given the diagnosis due to stigma associated with the same. Psychiatric comorbidity may well influence both the perception of NeuP and outcome of treatment with NeuP drugs. Concomitant treatment of psychiatric comorbidity may therefore have positive effects on neuropathic pain, and recent studies suggest that such treatment should be an integrated part of the treatment of neuropathic pain [18,19]. However, it has been argued that the main focus of such treatment should be with nonpharmacological strategies (e.g., cognitive behavioral therapy), and routine prescription of SSRI or benzodiazepines in this patient population is not recommended [18]. More effort should be directed toward giving accurate diagnoses to patients to ascertain optimal treatment and follow-up. This is especially important for patients with

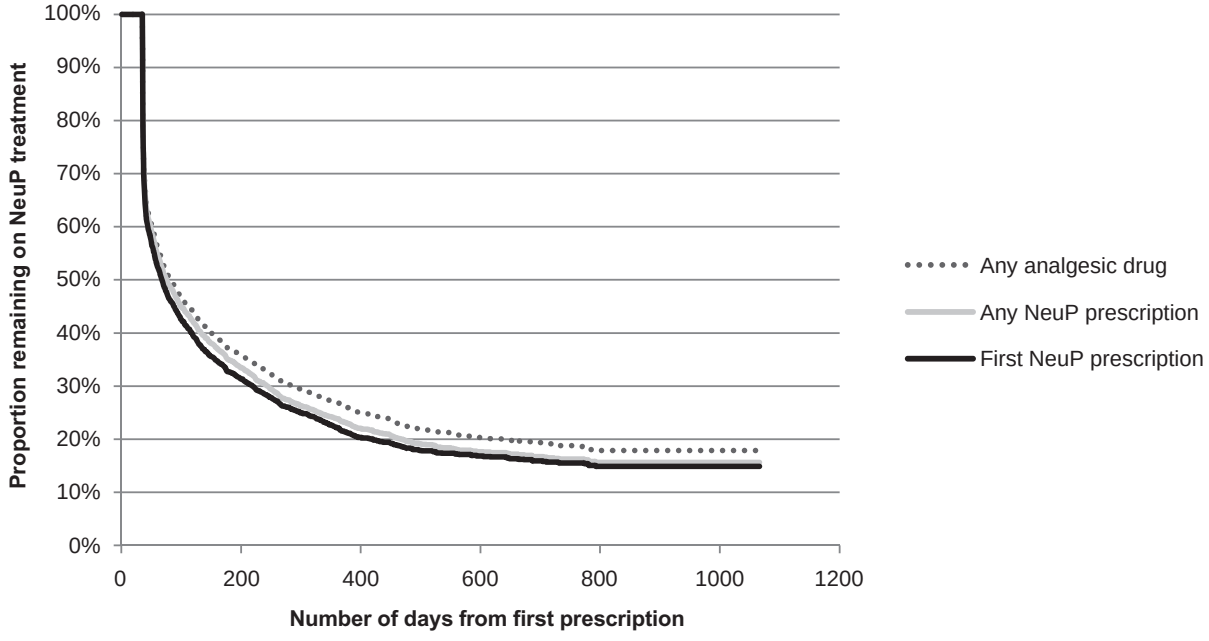

Figure 4 Proportion of patients on any analgesic drug treatment (including first and any pharmacological treatment indicated for neuropathic pain [NeuP]) over time (only considering those with a subsequent health care contact).

psychiatric comorbidities as they constitute more than half of those initiating treatment with a NeuP drug and because the presence of comorbidity should be central in the selection of treatment. Further research is needed, e.g., on the potential of the selection of drugs targeting both pain and anxiety/depression simultaneously (e.g., SNRI and TCA).

The three diagnosis groups were similar in terms of demographics and continuation rates. Small differences were seen in which drugs were prescribed. Anticonvulsants (pregabalin and gabapentin) were relatively more common in patients with neuropathies and mixed pain, while amitriptyline was relatively more common in patients with other diagnoses (although amitriptyline was the most common in all groups in absolute terms). The sequence of prescriptions corresponded with treatment guidelines in most patients, as amitriptyline was the most common first NeuP prescription, followed closely by gabapentin and pregabalin. However, it is worth noting that pregabalin was a relatively common first treatment which is not recommended in the Swedish guidelines.

Swedish recommendations further states that the prescription should be reevaluated after 3–6 months and terminated if possible [13]. Our data showed that about 60–70% of patients that were still in contact with health care had discontinued NeuP treatment after 6 months. This is more than what has been reported from clinical trials. Most trials are shorter but the few long-term trials available for duloxetine in patients with diabetic peripheral neuropathic pain report discontinuation rates in the range of 35–45% at 6 months [20,21]. Another of our findings was that most patients did not get a second prescription with an alternative drug when discontinuing their first. The reasons for discontinuing are not known but they are probably more often related to lack of efficacy or side effects (not least in relation to poorly managed expectations on, e.g., instant pain relief) than to improvement of symptoms. This assumption is supported by previous evidence of about 75% of patients with chronic painful diabetic neuropathy reporting pain of the same severity after 5 years [12], although this particular diagnostic group may have more severe and persisting symptoms than the more heterogeneous patients in our study. A reasonable interpretation is that many patients remain without adequate treatment of their pain which causes them reduced quality of life. Our findings are consistent with this notion although they do not provide any conclusive evidence of the same.

Patients starting on SNRI (duloxetine, venlafaxine) continued for longer compared with the TCAs and anticonvulsants. This may be due to differences in the patient populations being prescribed the different drugs, including differences in diagnoses and or severity of pain. Another possible explanation may be that treatment with SNRI is more successful, either by providing a better effect or less side effects.

This analysis is based on the complete patient population in a regional health authority in western Sweden (Västra Götalandsregionen). With 1.56 million inhabitants, they constitute a sixth of Sweden, and their treatment patterns may therefore be a valid indicator of Sweden as a whole. Furthermore, this study is based on the actual dispatches of the identified patients in the defined period of time, which implies that there is no uncertainty related to sampling in our findings. There are to our knowledge no previous studies on the prescription patterns over time of patients with NeuP in clinical practice.

The selection of patients has several limitations. First, the list of ICD-10 diagnoses to identify patients with a diagnosis related to chronic pain is comprehensive, and the diagnoses are not pain specific. That is, many of the diagnoses are also given to patients that do not suffer from pain although chronic pain is common in patients with each of these diagnoses [14]. Second, the NeuP drugs are indicated for other diseases than NeuP. We tried to refine our selection of patients to those with a higher likelihood to receive their prescription due to NeuP. This was the reason for excluding patients with a diagnosis of epilepsy or mood disorder. However, some patients with a mood disorder diagnosis may actually have received their prescription due to neuropathic pain. Furthermore, we did not exclude patients with anxiety disorders which may also be an indication for some of the NeuP medications (especially clomipramine and venlafaxine) [22,23]. Some patients that should have been included in the analysis were therefore excluded and vice versa. Third, the selected NeuP drugs are not exhaustive for the drugs indicated for neuropathic pain, but other drugs should be infrequent and was therefore of limited relevance for the study (e.g., carbamazepine and oxcarbazepine specifically indicated for trigeminal neuralgia). By the chosen methods, we believe we have identified most of the relevant patients for the undertaken analysis.

The stratification of patients into the three diagnosis groups is not clear-cut. There is variation and uncertainty in the origin of pain for patients with specific diagnoses, and certain diagnoses may therefore fit in several groups.

We did not have any information on the cause of treatment discontinuation, irrespective of whether it was caused by death, lack of efficacy, side effects, or relief of pain. In absence of mortality data, we censored patients when they no longer had a subsequent record in any of the administrative databases. As can be seen comparing Figures 1 and 2, this did not have a large effect on the proportions. Still, the analysis on treatment discontinuation is applicable for patients that are still in contact with health care.

Conclusions

Our findings suggest that long-term treatment with the currently available drugs indicated for neuropathic pain is not common in most patients. Fewer patients in clinical practice remain on their first prescription compared with findings from clinical trials, and surprisingly, few try more than one drug. Although not studied here, it is reasonable to assume that a large proportion of these patients still

suffer from pain with poor quality of life as a result. In addition to the need for better treatment options, we consider this to indicate a need for improved routines and guidelines on drug titration, follow-up, and switch of drugs. Furthermore, we consider the poor specification of neuropathy diagnosis and frequent psychiatric comorbidity both to be indications of a need for better routines in diagnosing patients to ascertain optimal treatment and follow-up.

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