Received: 19 February 2024 | Revised: 23 April 2024 | Accepted: 10 May 2024

DOI: 10.1002/ejp.2298

EJP European Journal of Pain

ORIGINAL ARTICLE

Prescribing pattern insights from a longitudinal study of older adult inpatients with polypharmacy and chronic non-cancer pain

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Abstract

Background: The present study sought to determine the prevalence of chronic non-cancer pain (CNCP) among older adult inpatients with polypharmacy. It also aimed to analyse prescription patterns and assess the therapy adequacy and patient complexity for those with and without CNCP.

Methods: This 4-year longitudinal study examined data from an exhaustive acute care hospital register on home-dwelling older adult patients (≥65) with polypharmacy. Commonly known combinations of potentially inappropriate medications were used to estimate therapy adequacy. Patient complexity was evaluated by comparing number of comorbidities and investigating physical and cognitive deficits.

Results: We determined a prevalence of CNCP of 9.7% among all older adult inpatients with polypharmacy, rising to 11.3% for those aged ≥85. Overall, CNCP patients were prescribed more drugs and had more comorbidities and physical and cognitive deficits than patients without CNCP. Older adult patients with CNCP received more analgesics, greater quantities of opioids, paracetamol and co-analgesics and elevated opioid dosages. Older adult patients with CNCP aged ≥85 received fewer analgesics, opioids, non-steroidal anti-inflammatory drugs and co-analgesics but more paracetamol. Older adult patients with CNCP were prescribed more potentially inappropriate medications involving opioids. In particular, 24.5% received an opioid and a hypnotic (benzodiazepine or Z-drug), and 8.6% received an opioid and a gabapentinoid.

Conclusion: Observed differences in medication use between older adult inpatients with or without CNCP may be relevant for clinical practice. Potentially inadequate co-prescribing (such as hypnotics and opioids) affects a higher proportion of patients with CNCP and may have serious unintended consequences.

Significance Statement: This study describes differences in prescription patterns between people with and without chronic non-cancer pain in a large dataset

of 20,422 discharges. The differences found may be relevant to clinical practice. In particular, high co-prescribing of opioids and hypnotics may have serious unintended consequences. Greater physical and cognitive deficits may indicate greater patient complexity, and appropriate interventions need to be developed to improve the management of this vulnerable patient group.

1 | INTRODUCTION

Chronic non-cancer pain (CNCP) may affect 28%–88% of older adults (individuals aged ≥65 years old) (Helme & Gibson, 2001), interfering with their physical and psychological well-being (Breivik et al., 2006). CNCP leads to reduced mobility, correlates positively with increased rates of depression and anxiety and strains relationships (Gloth, 2004). Furthermore, it exacts a substantial financial toll, with estimated annual direct and indirect costs ranging from USD 560 to 635 billion in the USA (Gaskin & Richard, 2012), EUR 200 billion in Europe (Barham, 2012) and CHF 4.3–5.8 billion in Switzerland (Oggier, 2007). In resource-limited countries, there are limited data on costs, but they are likely to be significant (Johnson et al., 2013).

The primary objectives of managing CNCP are effectively alleviating pain and maintaining or ideally enhancing functionality. CNCP management typically involves a complex regimen combining medications, physical therapy and psychological interventions (Schwan et al., 2019). While non-opioid medications, such as non-steroidal anti-inflammatory drugs (NSAIDs), have demonstrated pain control efficacy, their use with older adult patients is limited due to potential gastrointestinal bleeding and adverse effects on kidney and cardiac function (Gurwitz et al., 2003; Stillman & Stillman, 2007). Alternatives like paracetamol and metamizole exist, but paracetamol is less potent and limited data are available for metamizole. Metamizole may also rarely (1:1,000,000) cause agranulocytosis, a potentially lethal adverse drug event (ADE) (Huber et al., 2015). Consequently, opioids are considered when non-opioid options have unfavourable risk–benefit profiles or are contraindicated (Barber & Gibson, 2009). Co-analgesics, a category of drugs originally developed for different purposes but found to improve pain perception, are also commonly prescribed. These include antidepressants like tricyclic antidepressants (TCAs) and selective serotonin and noradrenaline reuptake inhibitors (SNRIs) and antiepileptic drugs like gabapentinoids (pregabalin or gabapentin) and carbamazepine (Saarto & Wiffen, 2007). However, attempts to manage CNCP may contribute to polypharmacy (Wise, 2013), increasing the risks of drug–drug interactions (Johnell & Klarin, 2007) and ADEs, including falls (Fried et al., 2014). In summary, addressing CNCP in older adults necessitates striking a delicate balance between achieving adequate pain relief and maintaining a safe medication regimen.

There is limited information on how to treat older adults with CNCP. While some evidence exists that analgesic drugs are associated with more complex drug regimens (Al-Qurain et al., 2020), it remains unclear whether this holds true for older adult patients with CNCP. It also remains uncertain how prevalent potentially inappropriate therapies in older adults with CNCP are, despite evidence suggesting that analgesics significantly contribute to ADEs among older adults (Barber & Gibson, 2009; Gurwitz et al., 2003).

Therefore, the present study's objectives were (1) to evaluate the prevalence of CNCP among a population of hospitalized older adults with polypharmacy, (2) to analyse and contrast prescription patterns for pain management and co-medications between patients with and without CNCP, (3) to explain these prescription patterns among different groups of older adult CNCP patients, specifically comparing the 'oldest old' (≥85) and those aged 65–84, and (4) to assess and compare therapy appropriateness and patient complexity between older adult patients with and without CNCP.

2 | METHODS

2.1 | Study design

This 4-year study (2015–2018) entailed a retrospective analysis of medical discharge records from a multi-site hospital in the French-speaking region of the Canton of Valais, Switzerland. We followed the STROBE reporting guidelines for cross-sectional studies (von Elm et al., 2007).

2.2 | Setting

This study was conducted at Valais Hospitals, a seven-site, acute care, public teaching hospital. It covers most surgical and medical disciplines, but not psychiatry, and overlaps two distinct linguistic regions (French

and German). In 2018, it served a population of around 340,000 and recorded over 40,000 hospitalizations and 480,000 ambulatory visits (Kanton Wallis, 2018; Spital Wallis, 2018).

2.3 | Eligibility criteria

Patient records were included if they met the following criteria: patients had to be aged ≥65, live in their own homes, be hospitalized at least once during the study period and have polypharmacy at hospital discharge. We defined polypharmacy as five or more prescribed medications, which is the most common definition (Masnoon et al., 2017). We selected home-dwelling patients with polypharmacy to focus on a vulnerable population that is especially sensitive to medication-related problems (Hauviller et al., 2016). Records were excluded if patients died during their hospitalization or their length of stay was <24 h, considered an ambulatory care visit in Switzerland.

2.4 | Data collection

The study's exhaustive dataset comprised routine patient data from medical records collected for administrative purposes. Each hospital stay had a unique identifier, as did each patient. Notably, our analysis focused on individual hospital stays as separate units of study; patient identifiers were not incorporated into the analysis. The dataset encompassed sociodemographic data, variables recorded throughout the hospitalization period and details documented at patient discharge. Variables recorded throughout the hospitalization included data on physical and cognitive function. Prescribed drugs were recorded at discharge. Additional information on how the dataset was created is documented elsewhere (Taushanov et al., 2021).

2.5 | Outcomes

2.5.1 | CNCP prevalence in hospitalized older adults

We calculated the prevalence of CNCP by dividing the number of older adult patients self-reporting it during their hospital stay by the number of older adults hospitalized at least once during the study period. Likewise, we calculated that prevalence among the 'oldest old', which we defined as patients aged ≥85.

CNCP patients were defined as patients who self-reported experiencing persistent or intermittent pain for 3 months and had no cancer diagnosis (we defined malignancies by prescriptions; see Supplementary Information 1). Patients with chronic cancer pain were included in the reference population. Nurses and physicians routinely screened all patients for chronic pain and recorded their responses in the electronic health record.

2.5.2 | Prescription patterns among older adult patients with and without CNCP

We compared the proportions of older adult inpatients receiving pain medication among patients with and without CNCP. We detailed pain medication use by specifying the proportions of patients in both groups prescribed paracetamol, NSAIDs, metamizole, weak opioids and strong opioids. We also described the proportions of patients using co-analgesics, including SNRIs, gabapentinoids, carbamazepine, muscle relaxants and hypnotics. Hypnotics included benzodiazepines and Z-drugs (zolpidem and zopiclone).

We calculated opioid strength in morphine milligramme equivalents (MMEs) according to the Centre for Disease Control and Prevention's recommendations (Dowell et al., 2022). As daily doses prescribed were missing from our database, we used defined daily doses, which are estimated based on the average maintenance dose per day for a drug used for its main indication with adults (WHO Collaborating Centre for Drug Statistics Methodology and Norwegian Institute of Public Health, 2023). In addition to MMEs, we also coded whether the opioid prescribed was categorized as weak or strong according to the World Health Organization's analgesic ladder for cancer pain relief (World Health Organization, 1996).

2.5.3 | Prescription patterns among the oldest old patients with CNCP

We followed the same methodology described above and compared proportions of older adult patients with CNCP using pain medications and co-analgesics by age group: 65–84 versus ≥85 years old.

2.5.4 | Adequacy of therapies and patient complexity among patients with or without CNCP

We defined potentially inappropriate drug combinations to assess therapy adequacy. Motter et al. (2018) synthesized explicit criteria for medication among older adults. We extracted the most commonly reported inappropriate drug combinations including an analgesic:

NSAIDs combined with angiotensin-converting enzyme (ACE) inhibitors, NSAIDs and diuretics, NSAIDs and corticosteroids, NSAIDs and anticoagulants/antiplatelet agents, NSAIDs and SSRIs, and TCAs and opioids. Because of their potential for ADEs, we also added opioids and hypnotics, and opioids and muscle relaxants (Boon et al., 2020; Dowell et al., 2022). We also added combinations of gabapentinoids and opioids because these can lead to increased sedation and opioid-related mortality (Gomes et al., 2017, 2018). Moreover, patients with CNCP treated using both opioids and gabapentinoids increasingly misuse gabapentinoids (Dowell et al., 2022; Smith et al., 2016). We also extracted Motter et al.'s most commonly reported inappropriate combinations of analgesics with other diseases (Motter et al., 2018), namely NSAIDs and renal diseases, NSAIDs and cardiovascular diseases, and NSAIDs and peptic ulcers. We compared the proportions of patients with potentially inadequate drug regimens among patients with and without CNCP.

We used the number of prescriptions as a proxy for patient complexity, as more prescribed medications lead to a greater potential for ADEs (Fried et al., 2014; Johnell & Klarin, 2007). We deduced underlying diseases by mapping prescribed medications' Anatomical Therapeutic Chemical (ATC) codes to disease classes (WHO Collaborating Centre for Drug Statistics Methodology and Norwegian Institute of Public Health, 2023). We used a framework based on an adapted version of the chronic disease score (Burgstaller et al., 2020; Kuo et al., 2011; Putnam et al., 2002). This framework distinguishes among chronic infections, chronic inflammatory diseases, diabetes, cardiac diseases, renal diseases, end-stage renal disease, gout, liver failure, organ transplants, thyroid diseases, neurological diseases, pulmonary diseases and psychiatric diseases. For an overview of disease–ATC code combinations, see Supplementary Information 1.

Complementing the analysis of comorbidities, we evaluated whether physical or cognitive function was impaired. Nurses routinely used a standardized drop-down menu on a tablet to collect patient-reported data on 17 domains of physical function and 5 domains of cognitive function. Values could be ordinal (comprising >2 categories) or binary (comprising two categories, i.e. present and not present). Domains of physical function included hearing, sight, speech, eating, drinking, urinating or defecating, mobility, physical exhaustibility and self-care. Mobility covered general impairments to mobility, limitations in changing body position, altered gait and the number of falls during the past year. Domains of cognitive function included vigilance, attention span, ability to learn and activities of daily living. The last variable described whether patients were oriented to person, place, time and situation.

We calculated an index summarizing a patient's physical and cognitive function to concisely describe their association with CNCP. To do so, we mapped each categorical value on a scale from 0 (no impairment) to 1 (complete impairment). For example, a score of 1 for the hearing variable represented a deaf patient, and 0 represented a patient with full hearing capacity. If a function was scored at an intermediate level, it was mapped on a discrete scale between 1 and 0 (i.e. 0.2, 0.4, etc.). We summed each patient's values for each variable and divided this by the number of variables to provide index ranges from 1, indicating no physical or cognitive function (complete impairment), to 0, indicating full physical or cognitive function (no impairment). For a detailed description, see Supplementary Information 2.

2.6 | Statistical methods

We imported the raw data and performed data cleaning before starting our descriptive statistical analysis using R statistical software (R Development Core Team, 2022a) and the tidyverse, lubridate, usethis, gitcreds, foreign, readxl and gtsummary packages (Csárdi, 2022; Grolemund & Wickham, 2011; R Development Core Team, 2022b; Sjoberg et al., 2021; Wickham et al., 2019; Wickham & Jreadxl, 2023; Wickham & Jusethis, 2022). We used descriptive statistics to assess the prevalence of CNCP, describe differences in prescription patterns between patients with and without CNCP and between CNCP patients aged 65–84 and those ≥85 and assess therapy adequacy and patient complexity. We reported the medians and interquartile ranges (IQR) of continuous variables and the percentage of patients within each category for categorical variables. We used the usual inferential statistical tests as indicators of the strengths of the relationships analysed: the Wilcoxon rank=sum, Pearson's Chi-squared and Fisher's exact tests, where appropriate. We considered *p*-values below 0.01 as significant. Only the cognitive and physical deficit information contained missing data. To calculate the previously described deficit accumulation indexes, we divided the number of deficits by the number of available parameters. We performed no data imputation.

3 | RESULTS

3.1 | CNCP prevalence

The dataset contained 20,422 discharges of 12,053 unique older adult inpatients, of whom 9702 (47.5%) were females. Median age was 79 (IQR: 73–85) years old. Further

characteristics are shown in Table 1. We identified a total of 1989 (9.7%) patients with CNCP, including 606 (11.3%) of 5350 patients aged ≥85 years. A total of 85 (0.4%) patients had chronic cancer pain.

3.2 | Prescription patterns among patients with and without CNCP

Patients with CNCP were prescribed a median of two analgesics (IQR: 1–3), whereas patients without CNCP were prescribed a median of 1 (IQR: 0–2) (Table 2). Patients with CNCP were prescribed more weak (22.6% vs. 15.7%) and strong opioids (28.6% vs. 9.6%) than patients without CNCP. The largest proportion of patients with CNCP (22.8%) received MMEs >90 mg, whereas the largest proportion of patients without CNCP (11.7%) received MMEs ranging from 15 to 50 mg. Paracetamol was more often prescribed to patients with CNCP (75.8% vs. 67.9%) than to those without it. Patients with CNCP were more often prescribed co-medications than patients without it, including more gabapentinoids (14.1% vs. 5.0%), TCAs (2.5% vs. 1.2%), SNRIs (3.8% vs. 2.0%), muscle relaxants (1.5% vs. 0.8%) and hypnotics (42.7% vs. 30.1%).

3.3 | Prescription patterns in the oldest old patients with CNCP

Among patients with CNCP, both the oldest old (aged ≥85) and those aged 65–84 were prescribed a median of two analgesics, but the younger group was often prescribed more than two different analgesics (IQR: 1–3), compared to the oldest old with an IQR: 1–2 (Table 3). We observed lower proportions of opioids, NSAIDs, gabapentinoids, TCAs, SNRIs, muscle relaxants and hypnotics among the oldest old patients than among those aged 65–84. In addition, the oldest old CNCP patients were also prescribed lower MMEs than younger CNCP patients. The oldest old patients were prescribed more paracetamol. Patients ≥85 were prescribed fewer co-medications. They were prescribed fewer gabapentinoids (8.1% vs. 16.7%), fewer TCAs (0.7% vs. 3.3%), fewer SNRIs (1.7% vs. 4.8%), fewer muscle relaxants (0.5% vs. 1.9%) and fewer hypnotics (34.8% vs. 46.1%).

TABLE 1 Study population characteristics.

Characteristic	$N = 20{,}422$[a]
Sex	
Women	9702 (47.5%)
Men	10,720 (52.5%)
Age (years)	
65–69	2702 (13.2%)
70–79	7957 (39.0%)
80–84	4413 (21.6%)
≥85	5350 (26.2%)
Median no. of prescribed drugs at discharge	9.0 (7.0, 12.0)
Median hospital length of stay (days)	8 (5, 14)
Median no. of readmissions	1.00 (0.00, 2.00)

[a]For categorical variables: *n* (%); for continuous variables: median (IQR).

3.4 | Therapy adequacy and patient complexity

Table 4 describes the adequacy of the analgesic therapies prescribed and shows the proportions of potentially inadequate drug–drug and drug–disease combinations for older adult inpatients with and without CNCP. Patients with CNCP were prescribed more potentially inadequate medications involving an opioid than were patients without CNCP, respectively, opioids and hypnotics (24.5% vs. 9.0%), opioids and gabapentinoids (8.6% vs. 2.2%), opioids and muscle relaxants (0.9% vs. 0.3%) and opioids and TCAs (1.6% vs. 0.4%).

Table 5 illustrates the patient complexity among patients with and without CNCP. Patients with CNCP were prescribed more drugs and suffered from more comorbidities. Patients with CNCP suffered significantly more often than those without it from inflammatory diseases (15.3% vs. 9.4%), liver failure (9.1% vs. 6.3%), neurological diseases (6.5% vs. 4.2%) and psychiatric diseases (33.8% vs. 23.5%). However, patients with CNCP were less afflicted by cardiovascular diseases (83.6% vs. 86.9%) and gout (3.2% vs. 4.4%).

Physical and psychiatric indexes differed significantly according to CNCP diagnosis. Patients with CNCP had a median of 0.18 (IQR: 0.08–0.35) deficits; those without CNCP had a median of 0.11 (IQR: 0.03–0.26) deficits. Both patients with and without CNCP had a median of 0.00 deficits regarding psychiatric function. However, older adult patients with CNCP had a significantly broader distribution of deficits (IQR: 0.00–0.12) than those without CNCP (IQR: 0.00–0.06).

4 | DISCUSSION

This 4-year study included a population of 12,053 unique older adult patients with 20,422 discharges, with polypharmacy and used nurse-led self-reported pain assessments. The prevalence of CNCP was 9.7%. The prevalence of CNCP among the oldest old (≥85 years old) was 11.3%.

TABLE 2 Prescription patterns for analgesics and co-medications across the whole study population and aggregated by a diagnosis of chronic non-cancer pain (CNCP). Bold *p*-values indicate significance, defined as being smaller than 0.01.

Characteristic	Overall, $N = 20{,}422$[a]	CNCP, $N = 1989$[a]	No CNCP, $N = 18{,}433$[a]	*p*-Value[b]
Analgesics	1.00 (1.00, 2.00)	2.00 (1.00, 3.00)	1.00 (0.00, 2.00)	**<0.001**
Opioid class				**<0.001**
Strong opioids	2342 (11.5%)	568 (28.6%)	1774 (9.6%)	
Weak opioids	3339 (16.4%)	449 (22.6%)	2890 (15.7%)	
MME				**<0.001**
0 < MME ≤ 15	131 (0.6%)	30 (1.5%)	101 (0.5%)	
15 < MME ≤ 50	2459 (12.0%)	308 (15.5%)	2151 (11.7%)	
50 < MME ≤ 90	1006 (4.9%)	188 (9.5%)	818 (4.4%)	
90 < MME	1894 (9.3%)	453 (22.8%)	1441 (7.8%)	
NSAIDs	1471 (7.2%)	136 (6.8%)	1335 (7.2%)	0.51
Metamizole	1758 (8.6%)	161 (8.1%)	1597 (8.7%)	0.39
Paracetamol	14,030 (68.7%)	1507 (75.8%)	12,523 (67.9%)	**<0.001**
Gabapentinoids	1201 (5.9%)	281 (14.1%)	920 (5.0%)	**<0.001**
TCAs	261 (1.3%)	49 (2.5%)	212 (1.2%)	**<0.001**
SNRIs	439 (2.1%)	75 (3.8%)	364 (2.0%)	**<0.001**
Carbamazepine	74 (0.4%)	8 (0.4%)	66 (0.4%)	0.76
Muscle relaxants	174 (0.9%)	29 (1.5%)	145 (0.8%)	**0.002**
Hypnotics	6392 (31.3%)	849 (42.7%)	5543 (30.1%)	**<0.001**

Abbreviations: Analgesics, number of analgesic drugs prescribed, including opioids, NSAIDs, paracetamol and metamizole; CNCP, chronic non-cancer pain; Hypnotics, benzodiazepines and Z-drugs (zolpidem, zopiclone); MME, morphine milligramme equivalent; NSAIDs, non-steroidal anti-inflammatory drugs; SNRIs, serotonin noradrenaline reuptake inhibitors; TCAs, tricyclic antidepressants.

[a]Median (IQR) for continuous variables; *n*/*N* (%) for categorical variables.

[b]Wilcoxon rank-sum test; Pearson's Chi-squared test.

Patients with CNCP were prescribed more analgesics and opioids and higher MMEs. They also received more paracetamol and co-analgesics. Among patients with CNCP, those aged ≥85 were prescribed fewer analgesics, opioids, NSAIDs and co-analgesics but more paracetamol than their counterparts aged 65–84. Patients with CNCP were also more likely to be prescribed potentially inadequate drug combinations involving opioid medications than patients without CNCP. The very high proportion of co-prescribed hypnotics and opioids was particularly concerning. Furthermore, older adult patients with CNCP had more complex drug regimens than those without, and these involved more prescriptions and comorbidities. Finally, patients with CNCP had more physical and cognitive deficits than those without.

We determined a prevalence of CNCP of 9.7% in our full older adult inpatient population and 11.3% among the oldest old. This aligned with a study of hospitalized patients aged ≥65 in Italy and Spain that reported a prevalence of chronic pain of 11.8% (Corsi et al., 2018). However, CNCP prevalence in those aged 65 and older has also been reported to reach 28%–88% (Helme & Gibson, 2001). It is worth noting that these studies are somewhat dated, which may affect the relevance of their findings to the current situation. In particular, the ageing of society or the opioid crisis should be considered as relevant influences. Data on CNCP are scarce in Switzerland. One survey observed that approximately 30% of nursing home residents aged ≥65 self-reported some form of pain (Gesundheitsobservatorium, 2015). Considering that roughly 50% of older adult patients indicating pain suffer from CNCP (Corsi et al., 2018), we can estimate that 15% of these nursing home residents may have CNCP. Therefore, our study found a lower prevalence of CNCP than expected from previous research. This highlights the need for appropriate screening and identification of CNCP using validated tools that take into account the cognitive status of older patients.

Older adult patients with CNCP were prescribed more opioids and higher MMEs than those without. Whether opioids are beneficial in CNCP management remains a point of discussion. Indeed, increasing evidence suggests that the risks of opioid use outweigh its benefits (Breivik & Stubhaug, 2014; Chou et al., 2009). Despite this, one study in the USA reported that 39.8% of patients with CNCP aged ≥65 were prescribed an opioid (Edlund et al., 2014), although little evidence exists that opioid doses >50 MME contribute much to pain relief (Chou et al., 2020). Indeed, the beneficial effects of opioids may plateau with doses

TABLE 3 Comparison of prescription patterns for analgesics and co-medications between CNCP patients aged 65–84 and those ≥85. Bold *p*-values indicate significance, defines as being smaller than 0.01.

Characteristic	65–84 years, $N=1383$[a]	≥85 years, $N=606$[a]	*p*-Value[b]
Analgesics	2.00 (1.00, 3.00)	2.00 (1.00, 2.00)	**<0.001**
Opioid class			**0.004**
Strong opioids	424 (30.7%)	144 (23.8%)	
Weak opioids	312 (22.6%)	137 (22.6%)	
MME			0.033
0 < MME ≤ 15	20 (1.4%)	10 (1.7%)	
15 < MME ≤ 50	208 (15.0%)	100 (16.5%)	
50 < MME ≤ 90	136 (9.8%)	52 (8.6%)	
90 < MME	340 (24.6%)	113 (18.6%)	
NSAIDs	119 (8.6%)	17 (2.8%)	**<0.001**
Metamizole	118 (8.5%)	43 (7.1%)	0.28
Paracetamol	1029 (74.4%)	478 (78.9%)	0.032
Gabapentinoids	232 (16.7%)	49 (8.1%)	**<0.001**
TCAs	45 (3.3%)	4 (0.7%)	**<0.001**
SNRIs	60 (4.8%)	10 (1.7%)	**<0.001**
Carbamazepine	8 (0.6%)	0 (0%)	0.12
Muscle relaxants	26 (1.9%)	3 (0.5%)	0.018
Hypnotics	638 (46.1%)	211 (34.8%)	**<0.001**

Abbreviations: Analgesics, number of analgesic drugs prescribed, including opioids, NSAIDs, paracetamol and metamizole; Hypnotics, benzodiazepines and Z-drugs (zolpidem, zopiclone); MME, morphine milligramme equivalent; NSAIDs, non-steroidal anti-inflammatory drugs; SNRIs, serotonin noradrenaline reuptake inhibitors; TCAs, tricyclic antidepressants.

[a]Median (IQR) for continuous variables; *n*/*N* (%) for categorical variables.

[b]Wilcoxon rank-sum test; Pearson's Chi-squared test; Fisher's exact test.

TABLE 4 Proportions of potentially inadequate drug–drug and drug–disease combinations among patients with and without CNCP. Bold *p*-values indicate significance, defined as being smal than 0.01.

Characteristic	CNCP, $N=1989$[a]	No CNCP, $N=18,433$[a]	*p*-Value[b]
Opioids and			
Hypnotics	488 (24.5%)	1605 (9.0%)	**<0.001**
Gabapentinoids	171 (8.6%)	404 (2.2%)	**<0.001**
Muscle relaxants	18 (0.9%)	59 (0.3%)	**<0.001**
TCAs	31 (1.6%)	67 (0.4%)	**<0.001**
NSAIDs and			
Anticoagulants	75 (3.8%)	862 (4.7%)	0.067
ACE-I/ATR	64 (3.2%)	536 (2.9%)	0.44
Diuretics	50 (2.5%)	328 (1.8%)	0.021
ACE-I/ATR and			
Diuretics	35 (1.8%)	232 (1.3%)	0.062
SSRIs	17 (0.9%)	113 (0.6%)	0.20
Corticosteroids	8 (0.4%)	35 (0.2%)	0.065
Renal insufficiency	1 (<0.1%)	9 (<0.1%)	>0.99
Cardiovascular diseases	106 (5.3%)	1029 (5.6%)	0.64
Peptic ulcers	109 (5.5%)	938 (5.1%)	0.45

Abbreviations: ACE-I/ATR, angiotensin-converting enzyme inhibitors or angiotensin receptor II antagonists; CNCP, chronic non-cancer pain; NSAIDs, non-steroidal anti-inflammatory drugs; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants.

[a]*n*/*N* (%).

[b]Pearson's Chi-squared test; Fisher's exact test.

>50 MME (Chou et al., 2020). The Centre for Disease Control and Prevention's Clinical Practice Guideline for Prescribing Opioids for Pain advises pausing and reassessing each individual's benefits and risks when considering prescribing doses >50 MME (Dowell et al., 2022). A recent study confirmed that higher MME doses independently increase the risk of emergency department visits and hospitalizations (Burgstaller et al., 2020) for trauma or overdose. Considering that opioid sales are increasing internationally (Müller et al., 2024; Wertli et al., 2017), policymakers and healthcare professionals should reconsider the value of managing CNCP using opioids. Consistent with other studies and contrary to current advice, opioids remain a cornerstone of CNCP management among older adults.

Studies on prescription patterns in the oldest old patients with CNCP are scarce. Evidence suggests that older adults are at a higher risk of undertreatment and pain-related disability (Barber & Gibson, 2009; Sawyer et al., 2006). Our study found that patients aged ≥85 with CNCP were prescribed fewer analgesics, strong opioids, NSAIDs and co-analgesics but more paracetamol. In contrast, a German study observed that patients with CNCP were prescribed more analgesics (metamizole and strong opioids) but fewer NSAIDs as they aged (Postler et al., 2018). Most guidelines agree that NSAIDs are potentially inappropriate drugs for older adults and discourage their use with patients older than 75 (American Geriatrics Society Beers Criteria® Update Expert Panel, 2023; Holt et al., 2010; Pazan et al., 2018). NSAIDs may result in acute kidney injury and chronic kidney disease, and they are associated with an increased risk of gastrointestinal bleeding (Davies et al., 2009; Pirmohamed et al., 2004).

Similarly, due to their side-effects profile, co-analgesics are often unsuitable for older adult patients (American Geriatrics Society Beers Criteria® Update Expert Panel, 2023; Holt et al., 2010; Pazan et al., 2018; Ungprasert et al., 2015). Paracetamol is often recommended as a safe analgesic choice for older adult patients with CNCP (Holt et al., 2010; Pazan et al., 2018) despite several high-quality randomized clinical trials have shown paracetamol to be non-superior to placebos (Nadler et al., 2002; Williams

TABLE 5 Indicators of patient complexity among patients with and without CNCP. Bold *p*-values indicate significance, defines as being smaller than 0.01.

Characteristic	CNCP, $N=1989$[a]	No CNCP, $N=18{,}433$[a]	*p*-Value[b]
Median no. of prescriptions	11.0 (8.0, 14.0)	9.0 (7.0, 12.0)	**<0.001**
Median no. of comorbidities	3.00 (2.00, 3.00)	2.00 (2.00, 3.00)	**<0.001**
Infections	0 (0%)	28 (0.2%)	0.11
Inflammatory diseases	305 (15.3%)	1738 (9.4%)	**<0.001**
Pulmonary diseases	233 (11.7%)	2147 (11.6%)	0.93
Renal diseases	38 (1.9%)	453 (2.5%)	0.13
End-stage renal diseases	23 (1.2%)	250 (1.4%)	0.46
Diabetes	359 (18.0%)	3697 (20.1%)	0.033
Liver failure	181 (9.1%)	1167 (6.3%)	**<0.001**
Transplant	25 (1.3%)	198 (1.1%)	0.46
Neurological diseases	130 (6.5%)	773 (4.2%)	**<0.001**
Gout	63 (3.2%)	819 (4.4%)	**0.008**
Cardiovascular diseases	1662 (83.6%)	16,014 (86.9%)	**<0.001**
Thyroidal diseases	239 (12.0%)	1910 (10.4%)	0.022
Psychiatric diseases	672 (33.8%)	4333 (23.5%)	**<0.001**
Physical index[c]	0.18 (0.08, 0.35)	0.11 (0.03, 0.26)	**<0.001**
Cognitive index[d]	0.00 (0.00, 0.12)	0.00 (0.00, 0.06)	**<0.001**

Abbreviation: CNCP, chronic non-cancer pain.

[a]Median (IQR) for continuous variables; *n*/*N* (%) for categorical variables.

[b]Wilcoxon rank-sum test; Fisher's exact test; Pearson's Chi-squared test.

[c]Physical index = Summary accumulated physical deficits score (0 = no deficits; 1 = all deficits).

[d]Cognitive index = Summary accumulated cognitive deficits score (0 = no deficits; 1 = all deficits).

et al., 2014). At the same time, paracetamol-induced liver injury may be underestimated (Roberts et al., 2016). Although our data indicate that physicians may indeed be following recommendations to decrease the number of potentially inadequate drugs and polypharmacy among the oldest old, this could result in decreased pain control and unfavourably impact their quality of life. Future studies need to assess the importance of our findings.

Patients with CNCP were prescribed more potentially inadequate drug regimens involving opioids than those without CNCP. Especially noteworthy was the number of co-prescribed opioids and hypnotics (23% vs. 9.2%), as current evidence suggests increased respiratory failure and mortality with these drug combinations (Boon et al., 2020). Similarly, patients with CNCP were more frequently prescribed the combination of gabapentinoids and opioids (8.0% vs. 2.3%) than patients without it, increasing the risk of overdose (Chou et al., 2020). Older adult patients with CNCP were also prescribed more drugs—the resulting polypharmacy has long been known to be linked with more medication-related problems (Johnell & Klarin, 2007), reducing quality of life (Duerden et al., 2013). This also aligns with our findings that patients with CNCP had more physical and cognitive deficits. Due to polypharmacy in general, and a higher occurrence of potentially inadequate drug combinations, the medication safety of older adult patients with CNCP may be compromised. Policymakers and healthcare professionals should focus on delivering high-quality care to older adult CNCP patients and improving their medication safety by carefully evaluating the need to co-prescribe potentially inadequate drug combinations.

4.1 | Strengths and limitations

The present study's primary strength was its use of an extensive database built upon an exhaustive hospital register. Second, the study aimed to describe current clinical prescription patterns and evaluate medication safety, and collecting routine data enables this. Third, our dataset contained variables, such as physical and cognitive deficits, that are rarely available in other datasets, allowing for innovative insights.

Nevertheless, the study had some limitations. First, nurses assessed chronic pain together with physical and cognitive deficits during hospitalization as part of a routine assessment. This was not performed using a validated CNCP screening tool and, thus, we suspect under-reporting of CNCP to be an important limitation of our study. As clinical assessments were not rigorously standardized (e.g. different assessors), we should expect higher variance. However, using routine data enabled an assessment of how

patients are treated in the real world. Second, we could not determine the precise indications or the duration of use of the reported medications. Especially in the case of co-analgesics, we did not know whether they were being used for their primary indications or as pain relief. As the analysis aimed to describe the current clinical picture, we do not believe that this diminished the clinical relevance of our results. Third, the study also lacked information on dosage regimens and therapy durations. To counter this problem, we followed an established procedure for estimating defined daily doses (WHO Collaborating Centre for Drug Statistics Methodology and Norwegian Institute of Public Health, 2023). However, this approach might not accurately reflect the clinically used doses, especially in older adults. Fourth, the reported prescribing patterns reflect trends at the time the study was conducted; trends may have changed since then. Fifth, data on cognitive and physical function were collected during hospitalization, not at discharge, and may not be representative of the true cognitive and physical status. However, we believe that these variables still serve as adequate proxies.

5 | CONCLUSION

The present study of home-dwelling older adult inpatients with polypharmacy at an acute care hospital found a prevalence of chronic non-cancer pain (CNCP) of 9.7% and described differences in pain medication use between those with CNCP and those without that may be relevant for clinical practice. For instance, patients with CNCP had more complex drug regimens, suffered from more comorbidities and had more physical and cognitive deficits indicating a need for greater medical attention. Potentially inadequate co-prescribing, such as the hypnotics and opioids co-prescribed to a high proportion (24.5%) of patients with CNCP, could have serious unintended consequences and should be regularly reviewed by clinicians. Patients with CNCP ≥85 years old were prescribed fewer non-steroidal anti-inflammatory drugs and opioids. This may indicate a reduced need for pharmacological treatment at older ages, or because they were prescribed fewer analgesics overall, these patients may be at a higher risk of being under-treated for CNCP. Further studies should analyse the potential risk factors for medication-related problems among CNCP patients and explore possible interventions to improve the quality of care for older adult patients with CNCP.

AUTHOR CONTRIBUTIONS

HV and BW set up the database. ANG and BW designed and performed the statistical analyses. All the authors developed the study methodology. All authors interpreted and commented on the results. ANG, MMW and CM-M drafted the manuscript. All the authors reviewed and approved the manuscript's final version. CM-M is the guarantor.

ACKNOWLEDGEMENTS

Open access funding provided by Inselspital Universitatsspital Bern.

FUNDING INFORMATION

The present study received no specific funding.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used and/or analysed during the current study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Goetschi, A. N., Verloo, H., Wernli, B., Wertli, M. M., & Meyer-Massetti, C. (2024). Prescribing pattern insights from a longitudinal study of older adult inpatients with polypharmacy and chronic non-cancer pain. *European Journal of Pain*, *00*, 1–11. https://doi.org/10.1002/ejp.2298