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**Describing long-term opioid use utilizing Nordic Prescription Registers –
A Norwegian example**

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Running title: Long-term opioid use in a Nordic prescription register

Keywords: opioids; long-term opioid use; pharmacoepidemiology; methods; Norway

Funding/Support: IO, VH, MH, and SS are funded in part by the Norwegian Research Council 320360

Abstract

Previous studies have defined long-term opioid use in varying ways, decreasing comparability, reproducibility, and clinical applicability of the research. Based on recommendations from recent systematic reviews, we aimed to develop a methodology to estimate the prevalence of use persisting more than three months utilizing one of the Nordic prescription registers. We used the Norwegian Prescription Register (NorPD) to extract data on all opioid dispensations between 1 January 2004 and 31 October 2019. New users of opioids (washout 365 days) were defined as long-term users if they fulfilled two criteria: 1) they had ≥ 2 dispensations of opioids, 91-180 days apart; 2) days 0-90 included ≥ 90 dispensed

This article has been accepted for publication and undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process which may lead to differences between this version and the Version of Record. Please cite this article as doi: 10.1002/bcpt.13706

administration units (e.g., tablets) of opioids. Overall, there were 2,543,224 new users of opioids during the study period. Of these, 354,666 (13.9%) fulfilled the criteria for long-term opioid use at least once. Compared with those who did not fulfill the criteria (short-term users), long-term users were older, more likely women, and used tramadol, oxycodone, and buprenorphine more frequently as their first opioid. In conclusion, we found that 1/7 of opioid users continued use longer than 3 months. Future outcome research should identify the clinically most important dose requirements for long-term opioid use criteria.

Introduction

The use of opioids has increased substantially in recent decades, especially in North America, Western Europe, and Oceania.¹ Opioids hold an important role in the treatment of severe acute pain and cancer pain, but the treatment of chronic non-malignant pain is controversial, as the risks of the treatment may outweigh the benefits.² In addition to risks commonly related to short-term opioid use, long-term opioid treatment has been shown to increase the risk of several severe adverse effects, including opioid use disorder and increased overdose-related mortality^{2,3}. The partially iatrogenic origins of the opioid epidemic in North America have increased concerns over potentially problematic patterns of prescription opioid use.⁴ Consequently, several studies have attempted to describe long-term opioid use and its determinants in different settings and various countries.⁵

There is no single agreed-upon clinical definition of long-term opioid use. Nevertheless, the most frequently applied definition, which is adopted by institutions such as the Centers for Disease Control (CDC) in the United States, parallels the definition of chronic pain: opioid use lasting more than 3 months.⁶ In epidemiological studies, the ways of defining long-term opioid use have varied widely, dramatically reducing comparability, reproducibility, and clinical applicability of this research.^{5,7,8} Models emulating opioid use persisting more than 90 days are the most frequently used, but how these models are constructed also differs.

Similar to global research, multiple studies have assessed long-term opioid use in the Nordic countries.^{9,10,19–21,11–18} All Nordic countries offer a similar potential to study opioid use from comprehensive, nationwide registers of prescription drug dispensations, or so-called prescription registers.²² However, previously conducted studies have defined their exposure very dissimilarly, with up to years of opioid use being required to qualify for “long-term use”. Moreover, requiring a certain dose is frequent in North American studies, where days’ supply is a common variable in claims-based data.⁷ However, in Nordic prescription registers, dose-related data are only included as a free text-based variable and is thus uncommonly used.²³

Three large systematic reviews from recent years have assessed the long-term opioid use definitions utilized in previous research, coming to similar recommendations for future studies: 1) a cut-off point of >90 days is preferred to define long-term opioid use, 2) consistency of the use should be assessed, and 3) sensitivity analyses assessing these definitions should be applied.^{5,7,8}

Primarily, we aimed to create a methodology to apply these recommendations to a Nordic setting. Secondly, we describe the prevalence of long-term opioid use utilizing this methodology among new users of opioids in Norway between 1 January 2005 and 31 October 2019.

Materials and methods

Data source

We utilized the Norwegian Prescription Database (NorPD) for this study.^{22,24} The NorPD includes data on dispensations from Norwegian community pharmacies from 2004 onwards with more than 99% completeness.²⁵ Each dispensation has been registered with personal characteristics and drug- and prescription-related information. Person-related information includes month and year of birth, gender, region of residence, and month and year of death, if applicable. Drug- and prescription-related information include a date of dispensation and a Nordic product number to identify the specific product. The dispensed amount is included as defined daily doses (DDDs), i.e., the assumed average maintenance doses per day when a drug is used for its main indication in adults, as defined by the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology.²⁶ In Norway, analgesic opioids are only available via prescription, and the NorPD, therefore, includes information on all opioid dispensations from community pharmacies. Conversely, this means that drugs used in hospitals and other institutions are not included in these data. All the persons in Norway with a valid personal identification number from 1 January 2004 to 31 October 2019 were eligible for this study. We extracted data from the NorPD on all opioid dispensations made during that period.

Opioids of interest

Drugs in the NorPD are registered according to the WHO Anatomical Therapeutic Chemical (ATC) classification system.²⁶ We included analgesic opioids (N02A) in this study, meaning opioids for opioid maintenance therapy (N07BC) or antitussives (R05DA), which have a main indication other than analgesia in Norway, were not included in the analyses. Administration forms were identified utilizing the Nordic product numbers. A list of the opioids included in this study is presented in Supplemental Table 1.

New opioid use definition and exclusions

All persons with at least one registered dispensation of opioids during the study period were considered the baseline population for this study. To study how long-term opioid use develops from new opioid use, we applied a washout period of 365 days, during which the study population was not allowed any opioid dispensations to be included in the final analysis (Figure 1). Because the data in NorPD starts from 1 January 2004, the incident opioid dispensation could at the earliest be on 1 January 2005. The first incident opioid dispensation was considered as the index date for all subjects in this study and only dispensations made after the index date could count towards long-term use periods. A person might have several incident dispensations (separated by 365-day periods without opioid dispensations), but only one index date (Figure 1). Long-term use was not required to start on the index date.

We excluded persons without a possibility to become long-term users. These were persons who had their index date less than 90 days before the end of the study period and persons who died within 3 months of their index date. Our data only included information on the month and year of death, so we considered either the first day of that month or the date of the last opioid dispensation that month as the date of death. All exclusions are shown in Figure 2.

Definition of long-term opioid use

Following the definition of chronic pain,²⁷ we aimed to model opioid use lasting more than three months as long-term use. In Norway, drugs used for long-term treatment are frequently reimbursed and dispensed for a maximum of three months at a time.²⁸ Consequently, a person using opioids for longer periods of time would need at least two dispensations between 91 and 180 days apart. To set a criterion for consistent use, we also required the long-term users to use at least one administration unit (e.g., a tablet) per day for the first 90 days, meaning at least 90 units needed to be dispensed within 90 days.

Due to their different administration pattern, the requirement for at least one administration unit per day for the first 90 days was different for transdermal opioids. Transdermal opioids, i.e., in Norway fentanyl and buprenorphine patches, are changed at even intervals. Therefore, we multiplied the number of patches by the number of days the patch is used for, i.e., 3 days for fentanyl and 7 days for buprenorphine patches. Since opioid patches are usually used one at a time, this number was increased by 20% to account for small gaps between pharmacy visits.²⁹ For liquids with concentrations corresponding to <10 oral morphine milligrams (MMEs) per milliliter, we assumed one unit to be 10 milliliters and for liquids with ≥ 10 MME/ml, one unit was assumed to be 1 milliliter. MMEs describe an equianalgesic dose of an opioid compared to oral morphine.³⁰

All incident opioid users, who 1) had one opioid dispensation and at least another one 91 to 180 days from the first one and who 2) were dispensed at least 90 units within 90 days from the first dispensation, were defined as long-term users (Figure 1).

A long-term use period ended either due to a gap of more than 180 days between two dispensations, death, or the end of the study period 31 October 2019. If a long-term period ended due to a gap between two dispensations, the last day of dispensation before the gap was considered the end of the long-term use period. A person could begin a new long-term use period only after another washout period of 365 days, i.e., after a new incident opioid dispensation. All persons who had at least one long-term use period were included in the cohort of long-term opioid users and all persons without a long-term use period in the cohort of short-term opioid users. The characteristics of the cohorts were measured at the index date.

Other characteristics of opioid users

In Norway, opioids can be prescribed with or without reimbursement. Importantly for the current study, they can be reimbursed for chronic pain and palliative care. This means the prescribing physician applies for the reimbursement on behalf of the patient, stating in the application that the patient meets a predefined set of criteria for a disease or medical condition. Reimbursement for the treatment is applied at the pharmacy.³¹ In NorPD, dispensations with reimbursement are detectable with specific reimbursement codes. In addition to demographics, we used these codes to identify opioid users with chronic pain and/or palliative care at the end of life to characterize the long- and short-term user cohorts.

Statistical analysis

We completed descriptive analyses using percentages, means with standard deviations (SDs), and/or medians with interquartile ranges (IQRs) when skewness was evident. Prevalence numbers during all of the follow-up period were derived by dividing the number of long-term users by the total number of opioid users included in the analyses. The incidence rate was computed by dividing the number of incident long-term users a given year by 1000

inhabitants. Population numbers were extracted from Statistics Norway.³² The year 2019 was excluded from this analysis due to incomplete data, i.e., end of the follow-up.

We estimated the duration of an opioid use period as the number of days between the first and the last dispensation adding the number of administration units on the last dispensation. Transdermal opioids were operated as described above. We then calculated three metrics of average treatment intensity within an opioid use period: units per day, DDDs per day, and MMEs per day. MMEs can be calculated from the DDD quantities included in the NorPD data with equianalgesic conversion factors. There is no single table of agreed-upon conversion factors for opioids; we utilized that supplied by the Norwegian Health Economics Administration.³³

We conducted several sensitivity analyses to ensure our results were not dependent on single variables. We applied different measures to both criteria for long-term use. These included extending and narrowing the time window of the second purchase from 90 days and increasing and decreasing unit requirements from one unit per day (i.e., 90 units) (Supplemental Table 2). Similarly, we applied alternative measurements to the number of administration units, mainly DDDs per day and MMEs per day. To estimate the effects of the prevalent user bias³⁴, we also conducted a sensitivity analysis in which no washout period was applied.

Additionally, we conducted a sensitivity analysis in which we classified the duration of opioid use modelling the clinical definition by the European Pain Federation: short-term (<90 days), intermediate-term (91-180), and long-term (>180 days).³⁵ Here, we applied the same logic as in the main analysis: long-term users were required to be dispensed ≥ 90 units between days 0-90, additional ≥ 90 units between days 91-180, and to have at least one dispensation on days 181-270. Intermediate-term users were thus those users who filled the main analysis criteria, but not the European Pain Federation's criteria for long-term use. For this analysis, we applied the same washout period and excluded persons without a possibility to become long-term users (those with less than six months of follow-up).

Furthermore, to estimate the one-year prevalence of long-term use among opioid users at any given year, the number of active long-term users who were dispensed an opioid that year was divided by the total number of persons who were dispensed an opioid that year. The year 2004 was not included in this analysis as opioid users were not able to fill the long-term criteria during the first 90 days. The year 2019 was not included due to incomplete data. Additionally, we calculated the prevalence rate in the population by dividing the number of long-term users a given year by 1000 inhabitants that year.

Because we have used full population data, we have not reported confidence intervals or significance testing, which are meant for describing uncertainty when estimating population values from smaller samples. All analyses were conducted using R, version 4.0 (R Foundation for Statistical Computing, Vienna, Austria. <https://www.R-project.org/>).

Results

Overall, 2,750,487 persons were dispensed an opioid during the study period (Fig 2.). Applying the washout and the exclusion criteria, 2,543,224 were new users of opioids. Of these, 354,500 (13.9%) filled our criteria for long-term opioid use at least once and were included in the cohort of long-term users, and 2,188,724 (86.1%) were included in the cohort of short-term users (Table 1).

Among long-term users, 56.6% were women and the median age at index date was 59 (IQR 43-73) with 60- to 79-year-olds being the largest 20-year age group (34.5%) (Table 1). Among short-term users, 51.4% were women and the median age was 45 (IQR 31-60) with 20- to 39-year-olds being the largest age group (34.0%). Approximately 7.0% of the long-term users and 0.1% of the short-term users received opioids reimbursed for chronic pain at some time point during the study period. Furthermore, 18.9% of long-term users and 1.6% of short-term users received opioids reimbursed for palliative care. At index date, codeine in combination products was the most frequently dispensed opioid to both long-term users (70.1%) and short-term users (75.9%), followed by tramadol (22.5% vs. 21.3%), oxycodone (2.3% vs. 0.9%), and buprenorphine (1.4% vs. 0.2%).

The first long-term period started at a median of 676 days (IQR 0-2021) after the index date. Approximately 28.7% (101,778) of long-term users began their first long-term user period from the first incident opioid dispensation (the index date). During the study period, there were 386,665 long-term opioid use periods, i.e., approximately 1.1 per long-term user (Table 2). The median age at the start of the long-term use was 62 (IQR 47-76) and the median number of days between the first and the last dispensation of a long-term use period was 498 (IQR 185-1335). Including the number of administration units in the last dispensation, the estimated median duration of a long-term use period was 553 days (IQR 246-1394). The long-term periods included a median of 1.2 units per day (IQR 0.8-2.0), a median of 0.3 DDDs per day (IQR 0.3-0.5), and a median of 4.5 MMEs per day (IQR 1.7-14.2). Approximately 4.5% of the periods included more than 100 MMEs/day and 0.9% more than 300 MMEs/day. On average, the opioids in a long-term period were prescribed by 4.7 physicians (SD 4.7). Approximately 15.6% of the long-term periods ended due to the person dying, 19.5% of the periods were estimated to continue until after the end of the study follow-up, and 65.0% ended due to a gap of more than 180 days between dispensations or due to no subsequent dispensations.

There were larger differences in the proportions of the first dispensed opioid when the start of the first long-term use period, rather than the index date, among long-term users was compared to the start of the first short-term use period (i.e., index date) of short-term users, (Figure 3). Similarly, there were considerable changes in the prevalence of different opioids over the years of follow-up. Although codeine in combination products remained the most frequently dispensed first opioid in both groups, its proportion decreased from 72.6% in 2005 to 43.7% in 2019 among long-term users and from 88.2% in 2005 to 60.0% in 2019 among short-term users. Conversely, the proportion of tramadol increased from 17.8% in 2005 to 35.5% in 2019 among long-term users and from 9.8% in 2005 to 34.5% in 2019 among short-term users. At the same time, the proportion of oxycodone among long-term users increased from 2.5% to 10.2%, and buprenorphine from 0.9% to 4.3%. Among short-term users, the

proportion of oxycodone increased from 0.2% to 3.3%, and buprenorphine from 0.1% to 0.2%.

In 2005-2018, the one-year prevalence of long-term use among all opioid users stayed stable varying between 24.4% and 25.4% (Table 3). The prevalence of long-term use in the population increased very slightly from 23.8/1000 inhabitants in 2005 to 25.7/1000 inhabitants in 2018. Similarly, the incidence rate of long-term use increased from 3.9 in 2005 to 5.8/1000 inhabitants in 2014, then decreasing to 5.0/1000 inhabitants in 2018.

Sensitivity analyses

Changes to either criterion changed the prevalence only slightly (Supplemental Table 2). A small threshold effect was found increasing the administration unit requirement during the first 90 days to over 100 (i.e., 1.1 units/day), which is a common number of tablets in a package (prevalence at 1.1 units/day: 13.7%; at 1.2 units/day: 11.8%). However, only requiring two dispensations, i.e., without unit requirements, increased the prevalence to 24.1%. Changing unit requirements to DDDs and requiring at least 1 DDD per day during the first 90 days resulted in a prevalence of 4.0%, whereas requiring at least 10 MME per day a prevalence of 7.7%. Using the main criteria, elimination of the washout period for the study population users increased the prevalence of long-term opioid use to 16.8%.

After the exclusions, there were 2,502,547 persons included in the analysis modelling the opioid use categories by the European Pain Federation. When these criteria were applied, 8.3% (208,634 persons) were defined as long-term opioid users at least once during the study period, 5.6% (140,307 persons) only as intermediate-term users, and 86.1% (2,153,606 persons) only as short-term users.

Discussion

In this study, we developed simple-to-apply criteria to investigate long-term opioid use utilizing drug dispensation data. Applying this methodology, we estimated that approximately 14% of all new opioid users in Norway became long-term users during our follow-up, with an incidence rate that varied between 3.9 to 5.8 per 1000 inhabitants. Compared with short-term users, long-term users were older, more often women, and used tramadol, oxycodone, and buprenorphine more frequently as the first opioid, with large changes throughout the follow-up period. A median long-term use period lasted more than 400 days, varying widely, with a relatively low dose measured in administration units, MMEs, and DDDs per day. The results of this study can further help to develop models of long-term opioid use especially with data from Nordic prescription registers or similar sources of drug dispensation information.

Our duration criterion for long-term opioid use was at least two dispensations, 91-180 days apart. Our estimate on the prevalence of long-term opioid use was higher than in previous Nordic studies that have required longer use periods.⁹⁻¹¹ Most other studies have also had specific populations, very commonly post-operative patients.^{12,13,15,19-21} Similarly to the current study, Quinn et al. (2019) studied long-term opioid use among all incident users in Sweden with requirements similar to ours, i.e., at two dispensations within six months, estimating its prevalence to 7.6%.³⁶ However, they did not include the so-called weak opioids into their analyses and did not require a minimum amount of opioids to be dispensed. Utilizing a minimum amount of opioids, researchers can reduce the risk of including persons

who have simply switched opioids due to adverse effects or lack of efficacy to their analyses, thus increasing the clinical applicability of their results.

The one-year prevalence of long-term use among all opioid users can be considered high, being approximately one in four throughout 2005-2018. In addition to including both prevalent and incident opioid users, the high number likely reflects the persistent nature of long-term use: the same individuals continue to use for multiple years, as can be seen in our estimates of opioid use duration. However, the stable trend of this prevalence is reassuring. Similarly, there were no large changes to either one-year prevalence or incidence rate of long-term use in the population. In addition to examining these trends closer, it is important to monitor the development beyond 2018, especially as the effects of the COVID-19 pandemic are difficult to forecast.

We argue that definitions estimating use longer than 90 days can be applied to a Nordic setting, especially as the most frequent duration of one dispensation in Finland, Norway, and Sweden is three months. If researchers prefer to prioritize other definitions, including sensitivity analyses utilizing the definition of “use longer than 90 days” is recommendable, as it increases comparability between studies and populations. One compromising possibility could be to model the categorization by the European Pain Federation,³⁵ where intermediate-term opioid use would have its own category. Our additional analysis showed intermediate-term users to be a sizeable part of the opioid using population.

The other criterion for long-term opioid use was a dose of at least 1 administration unit per day for the first 90 days. Similarly to ours, some previous Nordic studies have used estimates of dose in studies of long-term opioid use.^{10,37} We argue that this also decreases the risk of including opioid switchers and increases the clinical utility of the method. In our sensitivity analysis without this criterion, almost one fourth of the opioid users became long-term users during the study period, suggesting that many use opioids sporadically and inconsistently, which is less likely to cause the adverse effects associated with continuous long-term opioid use. Exactly what the minimum required dose should be and whether it should be measured in administration units, DDDs, or MMEs, could be studied in adverse outcome studies with varying opioid doses as exposure. However, it should be noted that DDDs frequently do not reflect actually used opioid doses and should therefore be utilized with caution in opioid research.³⁸ This discrepancy may also in part explain the low prevalence of long-term opioid use in our sensitivity analyses utilizing DDDs.

We found tramadol, oxycodone, and buprenorphine to be more frequently the first opioid among long-term users compared to short-term users of opioids. Short-term opioid users were dispensed overwhelmingly codeine in combination products, the most commonly used opioid products in Norway. It is likely that in addition to chronic pain and palliative care, other conditions causing severe pain are more common among long-term users of opioids. This more severe pain is likely the main reason why long-term users are prescribed stronger opioids more frequently than short-term users. However, all three opioids have also been associated with long-term use previously, in post-surgical patients.³⁹ Whether they increase the risk of long-term use independently in a general population, should be studied more carefully. This is especially important, as we found increasing trends of these opioids in both cohorts. Another possible finding of concern can be the number of prescribers, averaging almost 5 per long-term period. Having multiple prescribers has been associated with adverse

outcomes in the treatment of chronic pain and should ideally be avoided.⁶ It is also possible that some of the opioid users in our study have engaged in so-called doctor shopping, i.e., visiting multiple prescribers to increase the amount of opioids they were prescribed. However, these concerns need to be confirmed in future studies.

Strengths and limitations

A major strength of our study was the comprehensive register of dispensed prescription drugs that we utilized. The NorPD includes data on all opioids dispensed from community pharmacies in Norway during the study period. It is important to note, however, that drugs used in hospitals or other institutions are not included in this study, and we did not analyze opioids with the main indication other than analgesia that can in some cases be used for pain. It is also possible that some opioid use periods have continued in hospitals, other institutions, or abroad and have been misclassified as short-term. Studies with multiple data sources should consider taking these factors into account. As another limitation, our results on long-term opioid use are estimates: we cannot fully confirm that dispensed opioids were consumed or that the opioid consumption was consistent. However, it is more likely that continuous dispensations of opioids also indicate consumption. Moreover, data on dispensations are better estimates of drug use compared to prescriptions⁴⁰ and when compared to drug use questionnaires, data on dispensations are not prone to recall bias. As an additional limitation, opioid use period durations, and therefore intensity measures, are also only crude estimates and it is possible that opioid use continues outside the follow-up period. We also did not use data other than those in the NorPD, meaning we had no information on the existence or severity of pain, opioid indications, morbidity, or other healthcare use. We therefore cannot make any definite conclusions about issues such as appropriateness of the opioid treatment or opioid misuse. It is also likely that there were persons with chronic pain or palliative conditions that had not received drug reimbursements for these illnesses and were therefore not characterized as having these conditions.

Conclusions

In this study, we developed a method to identify long-term opioid use from a register of dispensed prescription drugs with relatively simple-to-apply criteria. Our analysis found that approximately 14% of all new users of opioids became long-term users within our study follow-up from 2005 to 2019. In line with recent international reviews, we recommend including a cut-off of more than 90 days of opioid use to identify long-term use, applying a minimum required dose, and using sensitivity analyses to both criteria.

Acknowledgements

None.

Conflicts of interests

None.

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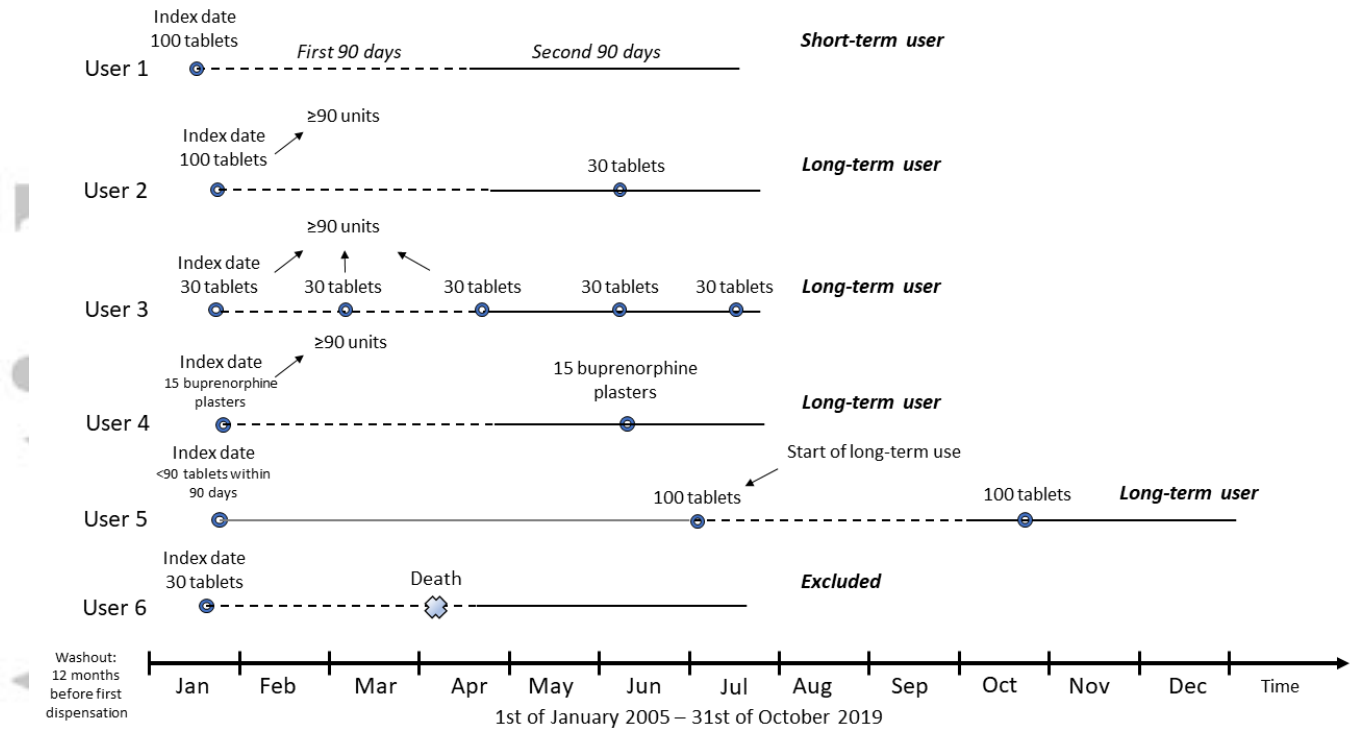


Figure 1. Study outline. New users of opioids were defined as long-term users if they 1) had a first dispensation and then a second one 91 to 180 days from the first one, and 2) were dispensed ≥ 90 administration units (e.g., tablets) of opioids within the first 90 days (Users 2, 3, and 4). Note that a person might have several incident dispensations (separated by 365-day periods without opioid dispensations), but only one index date. See Methods section for transdermal opioids (User 4) and exclusion criteria (User 6).

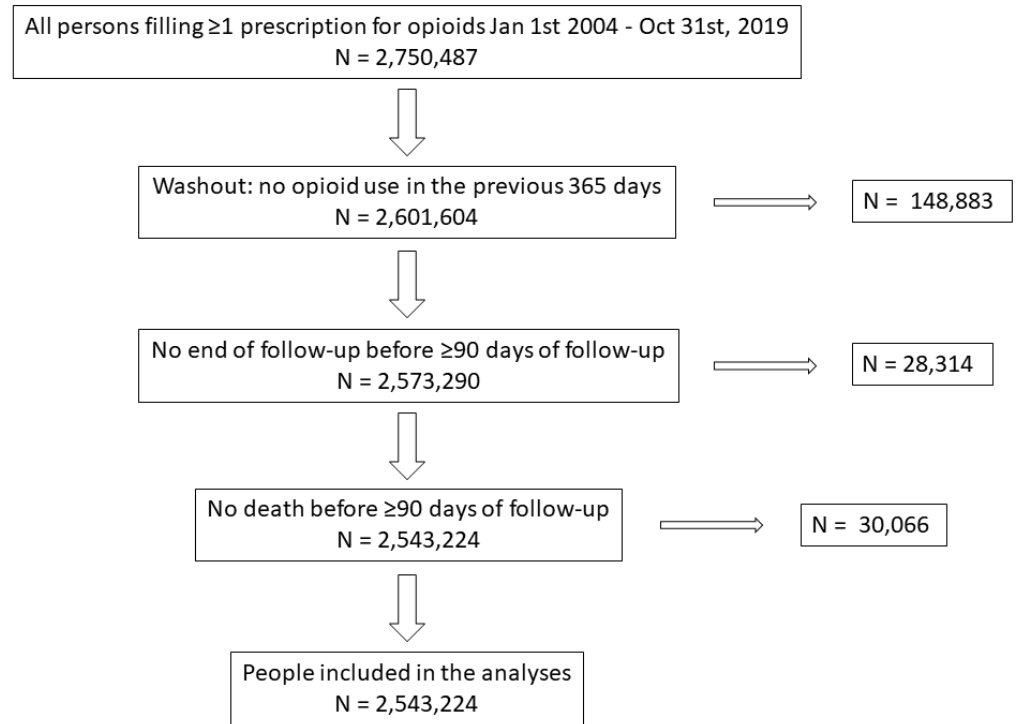


Figure 2. Study exclusions.

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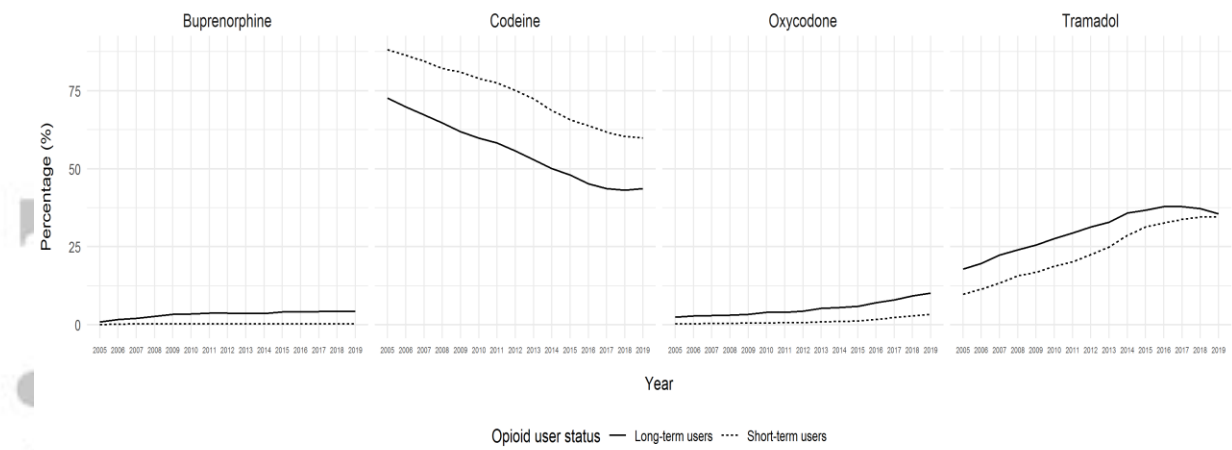


Figure 3. Proportion of the most frequently dispensed opioids at the start of the first long-term use period (long-term users) or at index date (short-term users) as a function of years of follow-up

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Table 1. Characteristics of long- and short-term users of opioids at index date.

	Long-term users	Short-term users
Total number of persons	354,500	2,188,724
Number of women (%)	200,543 (56.6)	1,125,771 (51.4)
Median age (IQR)	59 (43-73)	45 (31-60)
Age groups		
0-19 (%)	5244 (1.5)	140,646 (6.4)
20-39 (%)	64,250 (18.1)	744,265 (34.0)
40-59 (%)	114,391 (32.3)	739,789 (33.8)
60-79 (%)	122,455 (34.5)	448,096 (20.5)
80 and over (%)	48,160 (13.6)	115,928 (5.3)
Users with reimbursements for chronic pain (%)	23,601 (6.6)	1250 (0.1)
Users with reimbursements for palliative care (%)	66,834 (18.9)	35,461 (1.6)
Median index date	17th Jan 2008	20th Jan 2011
First opioid of the first long-/short-term period		
Codeine in combination products (%)	248,552 (70.1)	1,662,000 (75.9)
Tramadol (%)	79,716 (22.5)	466,694 (21.3)
Oxycodone (%)	8298 (2.3)	20,705 (0.9)
Morphine (%)	2672 (0.8)	3214 (0.1)
Buprenorphine (%)	5129 (1.4)	4982 (0.2)
Fentanyl (%)	1117 (0.3)	915 (0.0)
Other opioids (%)	4625 (1.3)	13,550 (0.6)
≥2 opioids at the same date (%)	4391 (1.2)	16,662 (0.8)

IQR = Interquartile range. Numbers for tramadol, oxycodone, and morphine include single-ingredient and combination products.

Table 2. Characteristics of long-term opioid use periods.

Mean age at the start of the first long-term use period (IQR)	62 (47-76)
Total number of long-term opioid use periods	386,665
Median number of days between first and last dispensation (IQR)	498 (185-1335)
Median duration of a long-term use period, days (IQR)	553 (246-1394)
Median number of days between long-term periods, if >1 (IQR)	2002 (1402-2790)
Mean number of DDDs per day per period (SD)	0.4 (0.7)
Median number of DDDs per day per period (IQR)	0.3 (0.2-0.5)
Mean number of MMEs per day per period (SD)	20.9 (64.9)
Median number of MMEs per day per period (IQR)	4.5 (1.7-14.2)
Mean number of administration units per day per period (SD)	1.7 (1.5)
Median number of administration units per day per period (IQR)	1.2 (0.8-2.0)
Long-term periods with >100 MME/day (%)	17,554 (4.5)
Long-term periods with >300 MME/day (%)	3499 (0.9)
Mean number of prescribers per period (SD)	4.7 (4.7)
Median number of prescribers per period (IQR)	3 (2-6)

IQR = Interquartile Range; MME = Morphine Milligram Equivalents; SD = Standard Deviation

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Table 3. Prevalence and incidence of long-term opioid use.

Year	Prevalence of long-term users among opioid users (%)	Prevalence of long-term opioid users per 1000 inhabitants	Incidence rate per 1000 inhabitants
2005	24.5	23.8	3.9
2006	25.0	24.3	5.0
2007	25.0	24.9	5.6
2008	25.1	25.5	5.7
2009	25.4	25.5	5.5
2010	25.4	25.5	5.3
2011	25.1	25.3	5.4
2012	24.8	25.3	5.5
2013	24.7	25.6	5.7
2014	24.8	26.0	5.8
2015	24.8	26.3	5.8
2016	24.8	26.5	5.7
2017	24.5	26.2	5.4
2018	24.4	25.7	5.0

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