Opioid analgesic use among Nova Scotia (NS) cancer patients at the end of life: results from a population-based study.

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Abstract

Cancer is a leading cause of morbidity and mortality in Canada and pain is a common management issue. Opioid analgesics are the mainstay of pharmacological therapy for moderate to severe pain because they are inexpensive, effective and easy to administer. Systematic analyses of population-level data on opioid use by cancer patients is limited in North America, however, Nova Scotia (NS) has clinical and administrative datasets to support such work. Opioid use was studied by linking data from two provincial health datasets: the NS Cancer Registry (NSCR); and the NS Prescription Monitoring Program (NSPMP) database. The end of life (EOL) sub-population includes all NS residents diagnosed with cancer from 1991 onward and living in NS who died between July 1, 2006 and December 31, 2010. The objective is to describe the prescription of opioid analgesics EOL period in the cancer disease trajectory. Univariate and multivariate analyses were used to describe drug use patterns at EOL, including number of prescriptions, morphine-equivalents/day, and chronic opioid use prior to death. Covariates included year of death, age group, sex, urban or rural residence, cancer cause of death, and survival prognosis. Among the EOL sub-population (n=11,498), 80% of prescriptions were for strong opioids, 18% for weak opioids, and 2% for other opioids. Variations in opioid use were observed in number of prescriptions dispensed, morphine-equivalents/day and duration of chronic treatment, particularly among younger patients and those with poorer prognosis cancer types. This study is the first of its kind in NS and provides a baseline understanding of the use of opioid analgesics among the NS cancer population at the EOL. This information can be used by CCNS and its stakeholders to identify focused areas for improving cancer pain management and allow exploration of areas that may benefit from ongoing monitoring.

Background

Cancer is a serious set of diseases with high incidence, prevalence and mortality in NS and across the globe. One well known consequence of cancer is pain associated with disease presentation and progression. Although there are many therapeutic options to cancer pain management, opioid use is one of the hallmark approaches, especially as pain becomes increasingly severe. This project is a population-based baseline study of opioid use among cancer patients during the 12 months preceding death (End of Life or EOL), using administrative databases to capture all cancer patients and all opioids prescribed through community pharmacies. The EOL study is nested within a larger study of overall opioid use among all NS residents diagnosed with cancer who received these medications in the June 2005 to December 2010 period.

Purpose

The study provides information on opioid dispensation patterns among EOL cancer patients, including the number of opioid prescriptions dispensed, average daily consumption (expressed as morphine equivalents per day), and the percentage that initiate chronic opioid use. Data was linked from the Prescription Monitoring Program (PMP), a program managed by Medavie Blue Cross on behalf of the Nova Scotia Department of Health and Wellness (NSDHW) with the Nova Scotia Cancer Registry (NSCR), managed by *Cancer Care Nova Scotia (CCNS)*. Linkage of data from different health-related administrative databases provides a means of obtaining important health system data not otherwise available. The resulting information will be used to better understand the burden of pain experienced among NS cancer patients and will facilitate treatment planning and decision making by those managing treatment protocols to improve the quality of life for these individuals.

Methods

The PMP Database

Pharmacists are required to submit data to the PMP on all opioid prescriptions that are dispensed in community pharmacies. The PMP is a standardized, electronically populated data system. The PMP dataset includes comprehensive drug, patient and prescriber related data such as drug name, type, dosage form and quantity dispensed, days' supply, patient sex and birth date and prescriber type.

The NSCR Database

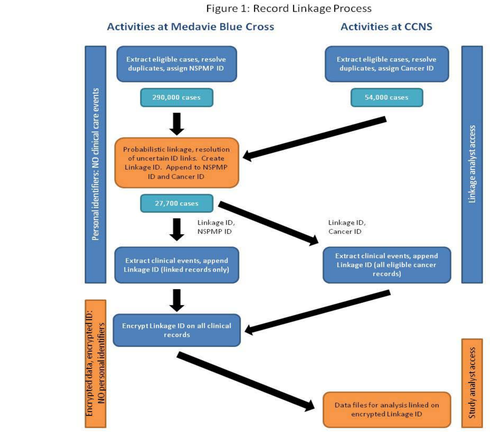
Cancer is a reportable disease in Nova Scotia. The NSCR has been collecting data on cancers diagnosed in the province since 1964. The International Classification of Diseases for Oncology is used as the standard classification system to define and categorize each new case. Additional reporting guidelines set out by the Canadian Cancer Registry at Statistics Canada are adhered to.

Record Linkage

Data linkage was undertaken using only identifiers necessary for probabilistic record linkage. No data elements such as prescription data or cancer treatment information were included at the data linkage stage. Figure 1 illustrates the record linkage process used to capture the entire study population (n=53,618 cases). The analytical data file for the EOL sub-population includes all NS residents diagnosed with cancer from 1991 onward and living in NS who had died between July 1, 2006 and December 31, 2010 (n=11,498 cases). Opioid prescriptions were restricted to those dispensed between June 2005 and December 31, 2010.

Methods

Figure 1: Record Linkage Process



Note: Use of PMP data outside of the program or with external partners for study purposes is new. Significant concerns existed on maintaining absolute confidentiality around individual level (person or prescriber based) prescribing data due to its sensitive nature, particularly around any inferences that might arise around inappropriate use. The final linkage process outlined above reflects an acceptable approach for all privacy reviewers involved in the study.

Study Outcome Variables

•**Number of Prescriptions** - for each cancer case, the sum of all opioid prescriptions dispensed within the one year period preceding death or from the date of diagnosis, if it occurred within the one year time period.
•**Morphine Equivalents per Day (MEQs)** - for each opioid prescription dispensed the MEQ is calculated by dividing the filled quantity by the days supply and multiplying the quotient by the morphine equivalent associated with the opioid in question. For oral solutions the filled quantity was divided by 5 to make them equivalent with tablet units. These values are summed for the one year period preceding death or from the date of diagnosis if it occurred within the one year time period and then divided by the total number of days to derive a daily average.
•**Chronic Opioid Use** - depending on the form of opioid, the calculation of chronic use differs. For tablets and oral solutions, chronic use was defined as use of 360 or more tablets/oral agents in a 90 day period. Use of controlled release agents automatically qualified as chronic use.

Study Covariates

•**Sex** (male, female);
•**Age Group at Death** (0-29, 30-39,40-49,…,80+).
•**Geographical Region** (urban, rural);
•**Cause of Death** (oral, esophagus, stomach, colorectal, pancreas, larynx, lung, skin, breast, cervix, body of uterus, ovary, prostate, bladder, kidney, brain, thyroid, non-Hodgkin's lymphoma, Hodgkin's lymphoma, leukemia, liver, multiple myeloma, other cancers, and non-cancer death). ICD-10 classification.
•**Prognostic Tier** 5-year survival probability (>80%, 50-80%, >80%).

Data Analysis

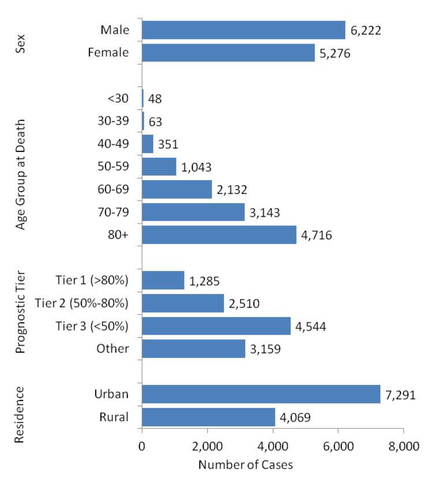
Univariate and multivariate analyses were used to describe opioid use patterns at EOL for each of the study outcome variables. The univariate analysis to estimate the number of opioid prescriptions dispensed within the study period used a person-days at risk method for each study covariate. Univariate regression analyses were used to estimate daily MEQ use for each study covariate. Univariate time-to-event analyses were used to estimate the percentage initiating chronic opiate use prior to death. This allowed for the systematic inclusion of the follow-up experience of all cases. The multivariate analyses controlled for the study covariates. All analyses were conducted using SAS 9.2.

Results

The EOL Study Population

The demographic and clinical characteristics of the EOL sub-population (n=11,498 cases) are shown in Figure 2. Males are slightly overrepresented (54% vs. 46% female). Approximately 87% were aged 60 and older at the time of their death. The most commonly occurring cancers (not shown) accounted for the following percentages of all deaths: lung (20%), colorectal (10%), prostate (4%), and breast (4%). Nearly two-thirds (63%) resided in urban areas at the time of diagnosis. Overall, 54% of the EOL sub-population were found in the PMP database.

Figure 2: Clinical and Demographic Characteristics of EOL Study Population (n=11,498)



Type and Quantity of Opioid Prescriptions Dispensed

Overall, 41,222 prescriptions were dispensed among the EOL sub-population, of which 89% were prescribed by a GP. The vast majority (81%) of prescriptions were for strong opioids such as hydromorphone (i.e., Diluadid™) (51%), and morphine (19%).

Number of Prescriptions

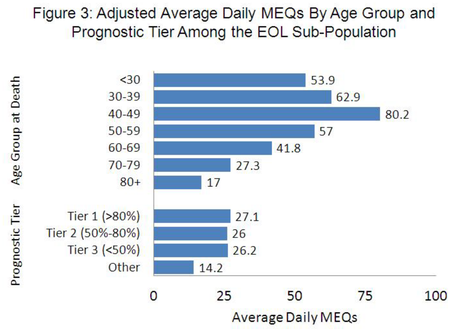
The univariate analysis of the number of opioid prescriptions dispensed within the study period showed significant variation by age group, cause of death, prognostic tier, and place of residence. Until age 50, increasing age was associated with more prescriptions; the reverse trend was evident from age 50 onwards. The number of prescriptions also increased with worsening prognosis. These findings remained statistically significant after controlling for the study covariates.

MEQs

Significant variation was also found in the univariate analysis of average daily MEQs by sex, age group at death, cause of death, and prognostic tier. The age effect was consistent with that for number of prescriptions. Average daily MEQs was similar across the prognosis tiers, however, the "Other" category (comprised of non-cancer deaths) show statistically different use of opiods. These findings remained after controlling for the study covariates (Figure 3).

Results

Figure 3: Adjusted Average Daily MEQs By Age Group and Prognostic Tier Among the EOL Sub-Population



Chronic Opioid Use

The percentage of EOL cases initiating chronic opioid use in the one year period preceding death varied significantly by age group at death, cause of death, and prognostic tier. The age group effect (Figure 4), observed previously for the number of prescriptions and average daily MEQs remained similar. The percentage of EOL cases initiating chronic use also increased with worsening prognosis (Figure 5).

Figure 4: Time to Initiation of Chronic Opioid Use By Age Group Among the EOL Sub-Population

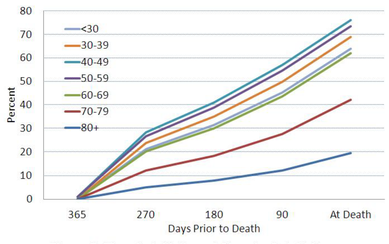
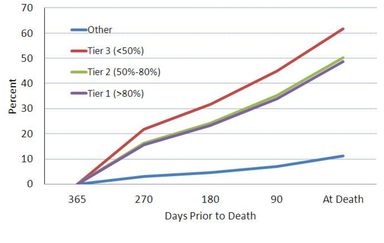


Figure 5: Time to Initiation of Chronic Opioid Use By Prognostic Tier Among the EOL Sub-Population



Conclusions

NS successfully linked the NSCR with a new source of confidential data from the NSPMP by using a two tier linkage process that addressed privacy concerns.
The study dataset allowed for key baseline information on cancer pain management in NS to be established e.g.
- Many prescribing patterns matched existing treatment guidelines.
- Age-effect pattern for 60+ individuals requires further study.
- GP's are target group for education.

The findings will be used by CCNS and its stakeholders to identify focused areas for improving cancer pain management and allow exploration of areas for ongoing monitoring or further study.