Predicting High Dose Opioid Utilizers: Different Models are Required for New and Current Opioid Users

PRIME THERAPEUTICS®

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Background

- The Office of Inspector General reported one in three Medicare Part D recipients had an opioid claim in 2017.[1]
- The Centers for Disease Control and Prevention (CDC) has identified high dose opioid therapy, greater than or equal to 90 milligram morphine equivalent (MME) daily dose, is associated with increased harm.[2]
- Many vendors sell opioid predictive modeling services to health insurers and health care providers. These vendors rely on health insurance claim information and/or electronic medical record data to identify individuals at increased probability of receiving high dose opioids. However, their predictive model data input, development process, independent predictors, and model performance are opaque.
- In a recent review of factors, methods and outcome definition in designing opioid abuse predictive models, only three studies have been done using claims data and all studies evaluate current opioid utilizers.[3] None of the studies identified predictors for new opioid users or assessed if the same predictive model techniques and predictors are appropriate when assessing opioid new users compared to current users.
- To our knowledge, there are no published administrative claims high dose opioid use predictive models focused on new opioid users.

Objective

- Identify opioid high dose predictors in Medicare members who are either new or current opioid users and determine if one predictive model can be used for both new and current opioid users or if separate models are needed.

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Methods

Input Data

- Prime Therapeutics (Prime) Medicare administrative claims pharmacy and eligibility data from 2015 through 2017 for approximately 1 million insured lives. Two different opioid utilizing cohorts were identified in 2016 to develop separate high dose opioid use predictive models for opioid new and current users. Members with cancer chemotherapeutic pharmacy claims or hospice indicator were excluded.
  - Opioid new user definition: members who received one or more opioid prescriptions between Jan. 1, 2016, and Dec. 31, 2016, and didn't fill any opioid prescriptions in the 180 days prior to their first opioid claim. The first opioid fill date represented the index date for each member.
  - Opioid current user definition: A 2016 date was first randomly assigned for all Medicare members, which represented the index date, and members needed to have at least one opioid claim 180 days prior to the index date.
  - High dose opioid use definition **(predictive model outcome)**: morphine milligram equivalent (MME) was calculated over six months from the index date using the Centers for Medicare and Medicaid Services (CMS) method.[4,5] All opioid claims during the 180 days are evaluated to determine if the member has an average MME ≥ 90 during their opioid use episode.

Over 170 potential predictors assessed

- Demographic variables, including age, gender, and ZIP code derived race, education and income
- Optum® Symmetry® Risk Groups® (PRG) score, proxy for severity of illness
- GuidedHealth® controlled substance score[6]
- Prescriber
  - Travel distance
  - Specialty (e.g., primary care, surgeon)
  - Prescriber is an opioid prescriber outlier
  - Prescriber shopping
- Pharmacy claims
  - Travel distance and pharmacy shopping
  - Index opioid claim — drug, MME, supply, long/short-acting, multiple opioid claims on index
  - Opioid claims history (for current users — 12 months from index date; for new users — claims seven to 12 months from index date); many opioid prior use volume and usage patterns assessed
  - Opioid refill too soon claim reject history
  - Benzodiazepine history
  - Muscle relaxant history
  - Other psychoactive drugs
  - Pharmacy benefit characteristics
  - Cost sharing and out-of-pocket (OOP) expenses
  - Days to opioid refill
- CMS member monthly file
  - Hospice (exclusion)
  - Low income status
- Two separate predictive models were built:
  - **New opioid users** — no opioid in past six months
    - Predicting MME ≥ 90 in the next six months
  - **Current opioid users** — 1+ opioid claims in past six months
    - Predicting MME ≥ 90 in the next six months

Predictive models assessed

- To predict if a member will receive ≥ 90 MME in the subsequent six months, two separate models, one for opioid new users and one for current users, were developed. Many models were tested and included, but not limited to:
  - Standard parametric (logistic regressions)
  - Nonparametric methods based on a decision tree (bagging and boosting methods were used)
  - Neural network
  - Random forests
  - Gradient boosting

Predictive model testing

- We randomly split the eligible sample into the three sub-samples of training (60%), validation (30%) and testing (10%). After a final model was identified using the training and validation subsamples, the predictive model was tested on the holdout sample to assess performance and potential overfitting.
- Independent predictors were assessed for correlation using variable inflation factor testing. Variable selection was made using R-square for continuous predictors and chi-square for categorical.
- The different predictive modeling methods were compared using c-statistic, sensitivity, specificity, and accuracy, with the most parsimonious model selected.

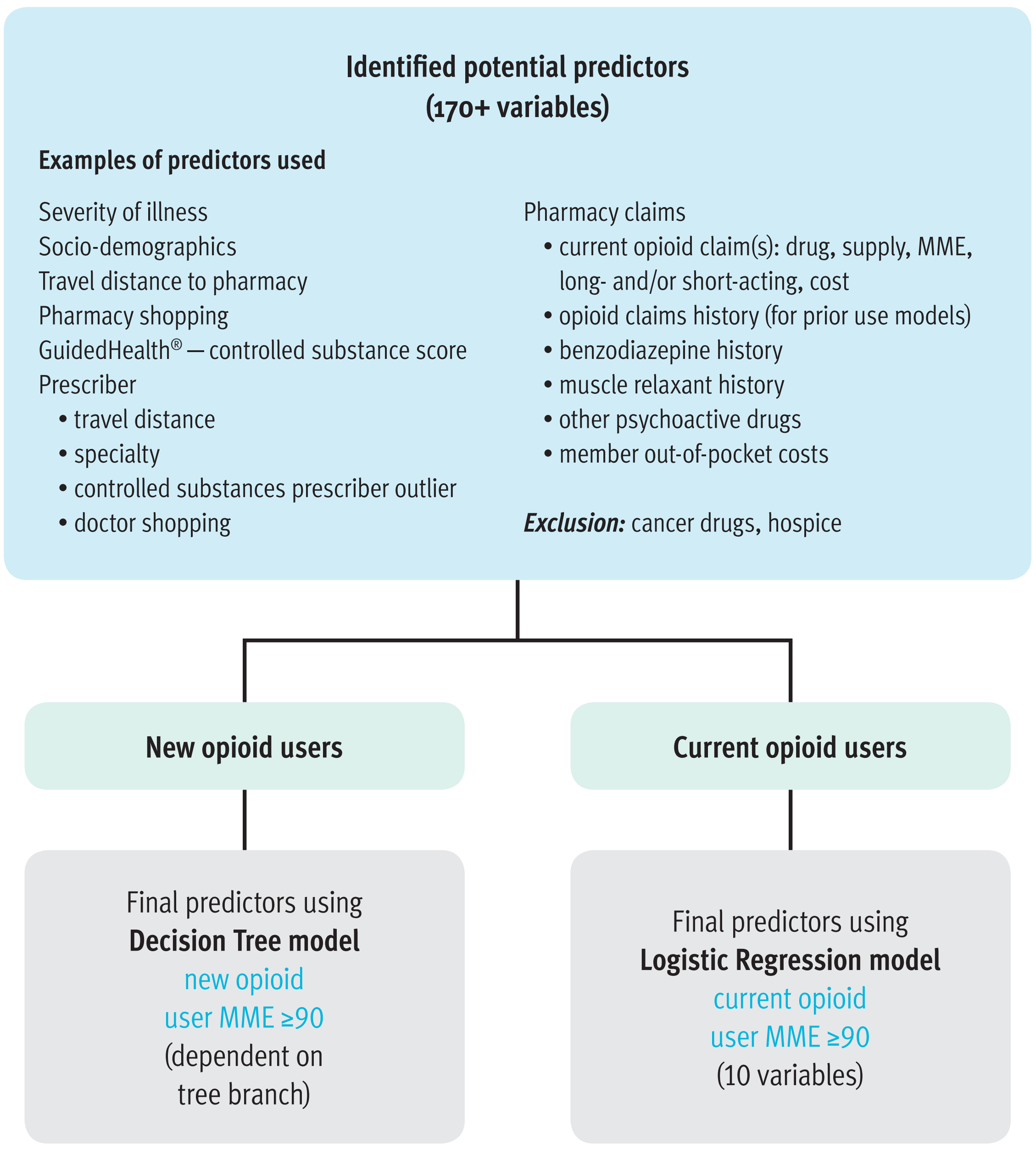
Results

- As of June 2018, Prime Medicare insured population of 1.3 million members had:
  - 442,286 (34%) with at least one opioid claim the past 12 months
  - 127,832 (10%) with an opioid claim in June 2018, 24,328 (19%) of the 127,832 were new opioid users
- This opioid predictive modeling research utilized Prime's 1 million Medicare members in 2016 to identify an opioid index date and found:
  - 265,594 **new opioid users,** of which 6,399 (2.4%) went on to have an MME ≥ 90 in subsequent six months
  - 273,328 **current opioid users,** of which 15,786 (5.8%) went on to have an MME ≥ 90 in subsequent six months
    - NOTE: 119,059 current opioid users transitioned from new opioid users in 2016

Best fitting predictive model (see Figure and Table)

- **New opioid users — Decision Tree** — C-statistic = 0.945
  - Top independent predictors are dependent on tree branch and include:
    - MME on index opioid claim
    - Long-acting opioid index claim
    - Day supply on index opioid claim
    - Long- and short-acting opioid claims on index date
    - Age under 65 years
    - Number of medications in claims history
    - Prescriber specialty (e.g., primary care, surgeon, etc.)
- **Current opioid users — Logistic Regression** — C-statistic = 0.973
  - Top independent predictors are:
    - Average MME in most recent month
    - Out-of-pocket (OOP) cost opioid claims expense, in past 12 months
    - Proportion of OOP for opioids out of all drugs OOP, in past 12 months
    - Prescriber specialty (e.g., primary care, surgeon, etc.)
    - Age under 65 years
    - Fentanyl
    - Oxycodone
    - Hydrocodone
    - Methadone
    - Morphine

Figure. Opioid Predictive Modeling — Best Fitting Model and Predictors are Different for New Users and Current Users



Identified potential predictors (170+ variables)

Examples of predictors used

Severity of illness
Socio-demographics
Travel distance to pharmacy
Pharmacy shopping
GuidedHealth® — controlled substance score
Prescriber
- travel distance
- specialty
- controlled substances prescriber outlier
- doctor shopping

Pharmacy claims
- current opioid claim(s): drug, supply, MME, long- and/or short-acting, cost
- opioid claims history (for prior use models)
- benzodiazepine history
- muscle relaxant history
- other psychoactive drugs
- member out-of-pocket costs

Exclusion: cancer drugs, hospice

New opioid users

Final predictors using **Decision Tree model** new opioid user MME ≥90 (dependent on tree branch)

Current opioid users

Final predictors using **Logistic Regression model** current opioid user MME ≥90 (10 variables)

Table. Medicare Members Opioid Morphine Milligram Equivalent (MME) ≥ 90 Predictive Model Diagnostics

New Opioid Users N = 79,679 from Validation Dataset

Actual occurrence over 6 months follow-up from index opioid claim using CMS methods[4,5]	Decision tree prediction	
	Predicted MME <90 N = 77,986 (97.9%)	Predicted MME ≥90 N = 1,693 (2.1%)
Observed MME <90 N = 77,759 (97.6%)	77,401 (99.5%)	358 (0.5%)
Observed MME ≥90 N = 1,920 (2.4%)	585 (30.5%)	1,335 (69.5%)

Accuracy = 98.9%
Specificity or True Negative Rate = 99.5%
Sensitivity or True Positive Rate = 69.5%
Precision or Positive Predictive Value = 78.9%

Negative Predictive Value = 99.2%
False Negative Rate = 30.5%
False Positive Rate = 0.5%
CMS = Centers for Medicare & Medicaid Services

Current Opioid Users N = 81,999 from Validation Dataset

Actual occurrence over 6 months follow-up from index opioid claim using CMS methods[4,5]	Logistic regression prediction	
	Predicted MME <90 N = 78,100 (95.2%)	Predicted MME ≥90 N = 3,899 (4.8%)
Observed MME <90 N = 77,263 (94.2%)	76,858 (99.5%)	405 (0.5%)
Observed MME ≥90 N = 4,736 (5.8%)	1,242 (26.2%)	3,494 (73.8%)

Accuracy = 97.9%
Specificity or true negative rate = 99.5%
Sensitivity or true positive rate = 73.8%
Precision or ositive predictive value = 89.6%

Negative predictive value = 98.4%
False negative rate = 26.2%
False positive rate = 0.5%
CMS = Centers for Medicare & Medicaid Services

Conclusions

- Although many vendors offer opioid risk assessment tools developed through predictive modeling, these vendors rarely provide a clear explanation of their data input, development process, independent predictors and model performance.
- Only three administrative data opioid predictive models have been published in the medical literature and none have been designed to predict high dose opioid use.[3]
- This Medicare opioid high dose predictive modeling work demonstrated separate modeling techniques were needed for new opioid users and current users. Independent predictors were different between the two models.
- These high dose opioid prediction models were sound with 98% + accuracy and specificity, and a clinically important true negative rate of greater than 99%.
- The true positive rate of 70% + allows for targeted interventions, especially early among new opioid users.
- It is essential separate modeling techniques for new and current opioid users are explored and tested when developing opioid predictive models.

Limitations

- Administrative claims include assumptions of members' actual drug use. In addition, the Prime administrative claim database is unable to see opioid prescriptions paid in cash or paid by another form of insurance, therefore misclassification bias exists.
- Medical claims, laboratory test results, and electronic medical record data were not included and may improve opioid predictive modeling.
- The data used in this study was limited to Medicare.
- New opioid users were defined as having no opioid claims in the past six months, a longer period of time without prior opioid use may result in different findings.
- The CMS opioid high dose use definition is one method to define high dose use, others exist. For example, the Pharmacy Quality Alliance (PQA) has an alternative opioid high dose use measure.[7]

References

1. HHS OIG Data Brief. Opioid Use in Medicare Part D Remains Concerning. June 2018. https://oig.hhs.gov/oei/reports/oei-02-18-00220.asp.
2. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016. MMWR 2016;65(1):1-49. doi:10.15585/mmwr.rr6501e1.
3. Alzeer AH, Jones J, Bair MJ. Review of Factors, Methods, and Outcome Definition in Designing Opioid Abuse Predictive Models. *Pain Med* 2018;19(5):997-1009.
4. CDC (Centers for Disease Control and Prevention). Calculating Total Daily Dose of Opioids for Safer Dosage. https://www.cdc.gov/drugoverdose/pdf/calculating_total_daily_dose-a.pdf. July 2017.
5. CMS. Improving Drug Utilization Review Controls in Part D. https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/RxUtilization.html.
6. Starner CE, Qiu Y, Karaca-Mandic P, Gleason PP. Association of a Controlled Substance Scoring Algorithm with Health Care Costs and Hospitalizations: A Cohort Study. *JMCP* 2016; 22(12): 1403-1410.
7. Pharmacy Quality Alliance (PQA). Use of Opioids at High Dose in Persons without Cancer. https://pqa.memberclicks.net/opioid-core-measure-set.