Understanding Predictors of Diagnosed Opioid Abuse: Predictive Model Development and Validation

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Humana-Pfizer Research Collaboration

Background

Introduction

Studies have reported the dramatic rate of increase in sales of opioids, which have paralleled the rise of opioid abuse and mortality associated with these drugs.[1-9] To attempt to curtail these numbers, incursions into the development of a model to predict abuse of opioids for chronic pain have been undertaken.[10-13] These types of models are important as a means to provide early identification of potential abusers and prevent this outcome rather than attempting to intervene after abuse has been diagnosed. However, to date, no one has documented the testing of a validated model in more than one national health plan, to ensure applicability and generalizability across the US.

Objective

- To develop and validate predictive models of diagnosed opioid abuse in the commercial member population of a national health insurance provider, Humana Inc.
- To test model stability using commercially available data.

Methods

- Two predictive models of opioid abuse were developed, validated and tested: 1) one for the overall population of members with opioid abuse diagnosis regardless of opioid use, and 2) another limited to a subset of members with a record of prescription opioid use prior to opioid abuse diagnosis.
- For model development, members newly diagnosed with opioid abuse in 2010 were identified using the following ICD-9-CM codes:
  - 304.0x – opioid type dependence
  - 304.7x – combination of opioid abuse with any other
  - 305.5x – opioid abuse
  - 965.0x – poisoning by opiates and related narcotics (excluding 965.01).
- The earliest date of diagnosis constituted the index date.
- Members were required to have 210 days of continuous enrollment pre-index, no prior diagnosis of opioid abuse or opioid poisoning, not be in a skilled nursing facility for ≥ 90 days, nor have claims for pregnancy.
- A random sample of commercial members without an opioid abuse diagnosis was identified in the 2010 data as a control group. A ratio of 5:1 (controls to cases) was used in developing the models.
- A stepwise logistic regression model was applied to a list of 24 variables considered to be potential risk factors. These included:
  - ≥ 1 opioid prescriptions, number of total pain medication prescriptions, number of opioid prescribers, RxRisk-V score (The RxRisk-V is a comorbidity index derived from drug claims data and has been validated to predict healthcare utilization and cost.[14,15])
  - Low back pain, neuropathic pain, other chronic pain, non-opioid poisoning, substance abuse, psychiatric diagnoses, Hepatitis A, B or C
  - ≥ 1 visit to a mental health specialist, ≥ 1 mental health inpatient admission, ≥ 1 emergency room visit
  - Age, gender, ethnicity, geographic region of residency.
  - Uncoordinated opioid use, multiple opioid trials, early opioid refills, excessive postsurgical opioid use, concomitant long-acting opioid use, morphine-equivalent dosing
- The resulting models were then tested using the data from the 2011 Humana commercial plan membership, and finally applied to a subset of the Truven Health Marketscan® Commercial Claims and Encounters dataset.

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Results

- For the overall 2010 sample, 10 variables were identified as being associated with being at risk for a diagnosis of opioid abuse (Table 1a) and 9 variables were identified for the subset of members with an opioid prescription (table 1b).

Table 1 Parameter estimates for multivariate model of opioid abuse

a. Overall Sample (n= 9,751)			
Parameter	Parameter Estimate	Adjusted Odds Ratio (95% Confidence Interval [CI])	P value
Total Number of Opioids	.174	1.19 (1.14, 1.24)	<.0001
Substance Abuse diagnosis	1.672	5.32 (4.07, 6.96)	<.0001
Psychological diagnosis	.859	2.36 (1.90, 2.93)	<.0001
Prescription for an Opioid	1.084	2.96 (2.41, 3.62)	<.0001
Age	-.031	.97 (0.96, 0.98)	<.0001
Total Number of Pain Medications	.059	1.06 (1.04, 1.08)	<.0001
Gender (Female)	-.190	.68 (0.59, 0.80)	<.0001
Low Back Pain diagnosis	.482	1.62 (1.31, 2.01)	<.0001
Hepatitis diagnosis	1.191	3.29 (1.36, 7.97)	.0084
Visit with a Mental Health Specialist	.370	1.45 (1.06, 1.97)	.0187
b. Subset of Prescription Opioid Users (n = 1,802)			
Parameter	Parameter Estimate	Adjusted Odds Ratio (95% Confidence Interval [CI])	P value
Total Number of Opioids	.183	1.20 (1.15, 1.26)	<.0001
Psychological diagnosis	.541	1.72 (1.29, 2.30)	.0002
Substance Abuse diagnosis	.958	2.61 (1.86, 3.66)	<.0001
Age	-.024	.98 (0.97, 0.99)	<.0001
Total Number of Pain Medications	.042	1.04 (1.02, 1.07)	.0004
Low Back Pain diagnosis	.433	1.54 (1.20, 1.98)	.0007
Visit with a Mental Health Specialist	.502	1.65 (1.05, 2.61)	.0308
Hepatitis diagnosis	.964	2.62 (1.02, 6.76)	.0458
Uncoordinated Opioid Use	.415	1.51 (.96, 2.39)	.074

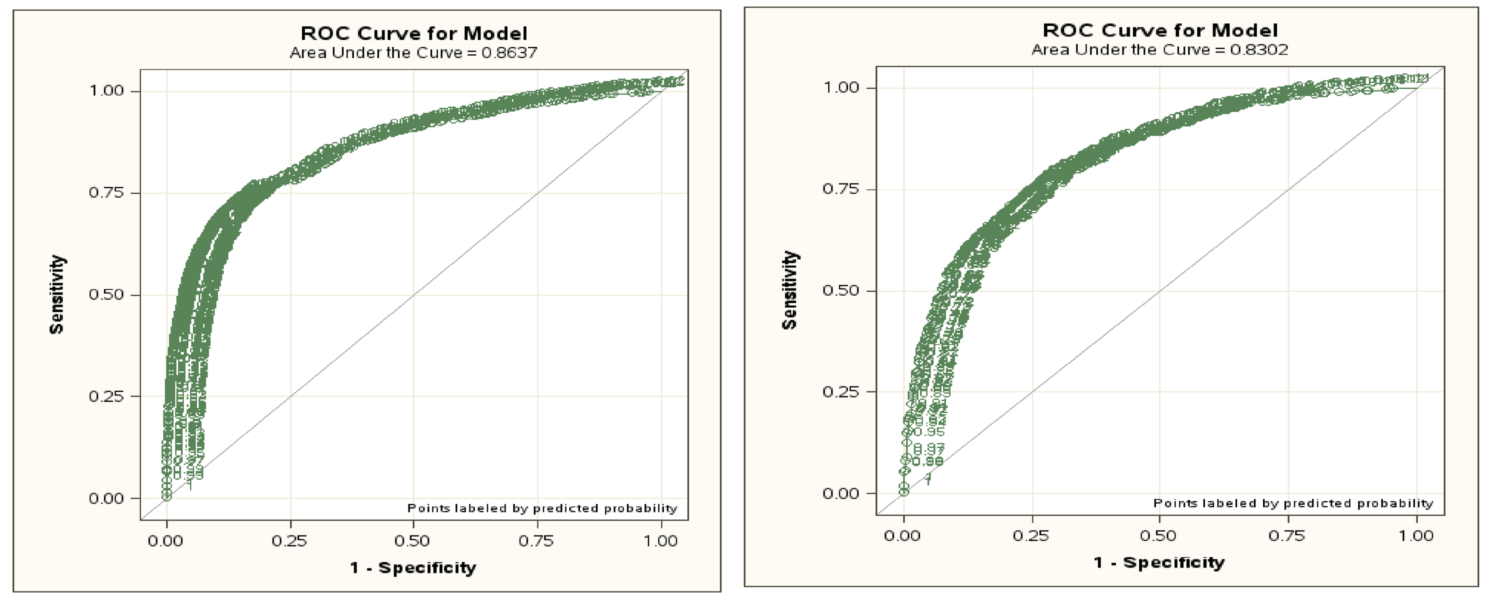
- The resulting overall model was applied to the original cohort (cases = 1,319) and had an accuracy (efficiency) of 88.4% at the cutoff level of ≥ .90 (Table 2a). The resulting model for the sub-cohort of opioid users (cases = 821) had an efficiency of 62.8% at the cutoff of ≥ .90 (Table 2b).
- As providers are sensitive to diagnose patients with opioid abuse, a key metric was a low false positive rate, i.e., scoring a member as at risk for a diagnosis of opioid abuse when no such diagnosis was found. A probability level ≥ .90 was deemed acceptable though it meant sacrificing sensitivity. The models' performance and fit statistics are reported in Table 2 (a and b) and ROC curves in Figure 1(a and b).

Table 2 Predictive model performance on original 2010 cohort (validation), and 2011 Humana membership (testing)

a. Overall Sample (2010) (optimized for False Positive)						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	10.6%	11.7%	15.9%	99.7%	88.4%	.864
b. Subset of Prescription Opioid Users (2010) (optimized for False Positive)						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	8.7%	40.4%	20.3%	98.4%	62.8%	.830
c. Overall Sample (2011) n=831,149						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	.3%	.25%	8.6%	99.7%	99.4%	.800
d. Subset of Prescription Opioid Users (2011) n=103,790						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	2.0%	.86%	14.9%	98.0%	97.2%	.805

Figure 1. ROC Curves, Model Development

a. Overall Sample **b. Subset of Prescription Opioid Users**



- The overall model was applied to the 2011 commercial membership that qualified for inclusion in the study (n=831,149; cases=2,248) and had an efficiency level of 99.4% at ≥ .90 (Table 2c). The model for the subset of members with a prescription for an opioid was applied to the 2011 commercial plan membership that qualified for inclusion in the study (n=103,790; cases=1,044) and had an accuracy of 97.1% at ≥ .90 (Table 2d).
- False positive rates observed at test were very low; however, the sensitivity rate of each model was also low. The *c* statistics at test were slightly lower than those obtained during model development (Table 2, a - d).
- The generalization of the models developed with data from 1 health plan were tested using the Truven dataset comprised of data from over 100 health plans. The models were applied to a random sample of 300,000 commercial members. The same variables identified using the Humana data were used and local coefficients for these variables were calculated using logistic regression. The resulting parameters approximated those described in Table 1 for the Humana cohorts and are displayed in Tables 3. The data were scored using the local coefficients. For the overall sample, the model achieved 99.7% accuracy (efficiency) at ≥ .90 (Table 4a).

Table 3 Parameter estimates for multivariate model of opioid abuse, Truven dataset

a. Overall Sample (n= 300,000)			
Parameter	Parameter Estimate	Adjusted Odds Ratio (95% CI)	P value
Total Number of Opioids	.084	1.09 (1.08, 1.10)	<.0001
Substance Abuse diagnosis	.893	5.96 (4.82, 7.37)	<.0001
Psychological diagnosis	.571	3.13 (2.51, 3.92)	<.0001
Prescription for an Opioid	.515	2.80 (2.26, 3.48)	<.0001
Age	-.024	.98 (.97, .98)	<.0001
Total Number of Pain Medications	-.004	1.00 (.99, 1.01)	.4051
Gender (Female)	-.259	.60 (.50, .72)	<.0001
Low Back Pain diagnosis	.231	1.59 (1.25, 2.01)	.0001
Hepatitis diagnosis	.575	3.16 (1.67, 5.99)	.0004
Visit with a Mental Health Specialist	.327	1.92 (1.50, 2.47)	<.0001
b. Subset of Prescription Opioid Users (n= 47,825)			
Parameter	Parameter Estimate	Adjusted Odds Ratio (95% CI)	P value
Total Number of Opioids	.097	1.10 (1.09, 1.12)	<.0001
Psychological diagnosis	.371	2.10 (1.56, 2.84)	<.0001
Substance Abuse diagnosis	.817	5.13 (3.93, 6.70)	<.0001
Age	-.036	.96 (0.96, 0.97)	<.0001
Total Number of Pain Medications	.006	1.01 (1.00, 1.02)	.3024
Low Back Pain diagnosis	.039	1.08 (.81, 1.45)	.6026
Visit with a Mental Health Specialist	.359	2.05 (1.48, 2.83)	<.0001
Hepatitis diagnosis	.359	2.05 (.85, 4.96)	.1111
Uncoordinated Opioid Use (Inefficiency)	-.895	.17 (.12, .23)	<.0001

- Applying the model for opioid users to the subset of prescription opioid users from the Truven dataset (n=47,825) achieved a 98.9% accuracy level at ≥ .90 (Table 4b).

Table 4 Test of predictive model performance on Truven commercial dataset

a. Overall Sample (2011) n=300,000						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	.2%	.15%	9.4%	99.8%	99.7%	.817
b. Subset of Prescription Opioid Users (2011) n=47,825						
Cutoff	False Positive	False Negative	Sensitivity	Specificity	Efficiency	C statistic (AUC)
≥ .90	.6%	.55%	9.3%	99.4%	98.9%	.886

Discussion and Recommendations

- This study demonstrated that predictive models of opioid abuse developed and tested using Humana data can be applied successfully to other health plans without loss of model performance.
- The risk factors identified are consistent with the published literature that reported the following as important risk factors related to opioid abuse and/or misuse: history of visits with mental health specialists, and psychological, substance abuse, or hepatitis diagnoses.[11,13] However, one important limitation of these published studies was that the timing of the opioid abuse diagnosis appeared irrelevant to when risk factor data for the predictive models were collected. Any intervention designed and implemented with the goal of prevention in mind would need to rely on risk factor identification well before the potential diagnosis.
- In order to confirm the clinical and economic value of implementing any intervention programs intending to address the underlying causes that increase the likelihood of diagnosed opioid abuse, the following steps are suggested when applying the predictive model to health plans generally:
  - Conduct a multivariate logistic regression analysis for the specific health plan of interest, using variables in Table 1, and compare parameter estimates to those from Humana's model reported in Table 1.
  - When testing the model, utilize plan-specific coefficients to predict the risk of diagnosed opioid abuse.
  - Determine whether members accurately predicted to be diagnosed with opioid abuse (or their providers) will be responsive to interventions and custom design interventions taking this knowledge into consideration.

Limitations

- The tradeoff between specificity and sensitivity was continually examined during model validation and testing. One limitation of opting to minimize the rate of false positives was the consequence that the model did not flag as many cases as hoped. Given this tradeoff, further examination of a higher number of false positive cases is needed to determine if their pattern of utilization warrants closer attention and monitoring, even in the absence of a diagnosis of opioid abuse in their observable future.
- Limitations common to studies using administrative claims data may be applicable to the current study, and may include lack of certain information in the database (e.g., lab results, weight, and health behavior information) and error in claims coding. No causal inference can be ascertained from this study, as it is an observational study using retrospective claims data. Although multivariate regression modeling was used to reduce selection bias and strengthen the causal inference, this approach can only reduce bias caused by measured covariates. It cannot reduce bias caused by unmeasured covariates.

Conclusion

This study presents predictive models of diagnosed opioid abuse that can easily be applied to any US health plan in order to identify members at risk for diagnosed opioid abuse. Once identified, health plans can implement targeted intervention plans to reduce abuse behaviors, ultimately curbing the rise in the rate of diagnosed opioid abuse across the US.

References **1.** Sehgal N, Manchikanti L, Smith HS. Prescription opioid abuse in chronic pain: a review of opioid abuse predictors and strategies to curb opioid abuse. *Pain Physician.* Jul 2012;15(3 Suppl):ES67-92. **2.** National Center for Health Statistics, 2006. Health, United States, 2006 with chartbook on trends in the health of Americans. In: Statistics NCfH, ed. Hyattsville, MD2006:68-71 **3.** Manubay JM, Muchow C, Sullivan MA. Prescription drug abuse: epidemiology, regulatory issues, chronic pain management with narcotic analgesics. *Primary care.* Mar 2011;38(1):71-90, vi. **4.** McAdam-Marx C, Roland CL, Cleveland J, Oderda GM. Costs of opioid abuse and misuse determined from a Medicaid database. *Journal of pain & palliative care pharmacotherapy.* Mar 2010;24(1):5-18. **5.** Manchikanti L. Prescription drug abuse: what is being done to address this new drug epidemic? Testimony before the Subcommittee on Criminal Justice, Drug Policy and Human Resources. *Pain physician.* Oct 2006;9(4):287-321. **6.** Sullivan CR. Opioid dependence. *The West Virginia medical journal.* Mar-Apr 2008;104(2):26-27. **7.** Boudreau D, Von Korff M, Rutter CM, et al. Trends in long-term opioid therapy for chronic non-cancer pain. *Pharmacoepidemiology and drug safety.* Dec 2009;18(12):1166-1175. **8.** Hahn K, L. . Strategies to Prevent Opioid Misuse, Abuse, and Diversion That May Also Reduce the Associated Costs. *American Health & Drug Benefits* 2011;4(2):107-113. **9.** Manchikanti L FB, Ailinani H, Pampati V. Therapeutic use, abuse, and nonmedical use of opioids: a ten-year perspective. *Pain Physician.* 2010;13(5):401-435. **10.** Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: a prospective cohort study. *BMC health services research.* 2006;6:46. **11.** White AG, Birnbaum HG, Schiller M, Tang J, Katz NP. Analytic models to identify patients at risk for prescription opioid abuse. *The American journal of managed care.* Dec 2009;15(12):897-906. **12.** Sullivan MD, Edlund MJ, Fan MY, Devries A, Brennan Braden J, Martin BC. Risks for possible and probable opioid misuse among recipients of chronic opioid therapy in commercial and medicaid insurance plans: The TROUP Study. *Pain.* Aug 2010;150(2):332-339. **13.** Rice JB, White AG, Birnbaum HG, Schiller M, Brown DA, Roland CL. A model to identify patients at risk for prescription opioid abuse, dependence, and misuse. *Pain medicine.* Sep 2012;13(9):1162-1173. **14.** Sloan KL, Sales AE, Liu CF, et al. Construction and characteristics of the RxRisk-V: a VA-adapted pharmacy-based case-mix instrument. *Med Care* 2003; 41: 761 – 774. **15.** Farley JF, Harley CR, Devine JW. A comparison of comorbidity measurements to predict healthcare expenditures. *Am J Manag Care* 2006; 12: 110-17.

Disclosures

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- **Conflicts of Interest:** Robert Dufour, Margaret Pasquale, and Nick Patel are employees of Comprehensive Health Insights, a wholly owned subsidiary of Humana Inc., who were paid consultants to Pfizer. George Andrews is an employee of Humana Inc. Jack Mardekian and David Schaaf are employees and stockholders of Pfizer Inc.