Predicting Opioid Dependency - Journey from Model to Paper

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EXPRESS SCRIPTS®

Today's Topics for Discussion

1. Introduction
2. Opioid Dependency Epidemic
3. The Model
4. Publication

An introduction

- MS in Industrial Engineering, Arizona State University
- Advanced SAS Certified
- 10 years experience:
  - Machine learning
  - Predictive modeling
  - Text analytics
  - Deep Learning
- Worked in various industries:
  - Credit card
  - Fraud detection
  - Healthcare
- Express Scripts since 2011

Putting medicine within reach

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MEMBERS

1.3 Billion
PRESCRIPTIONS PER YEAR

3,000
CLIENTS

$102 Billion
2015 REVENUE

27,000
EMPLOYEES

» National Leader in Pharmacy Benefits

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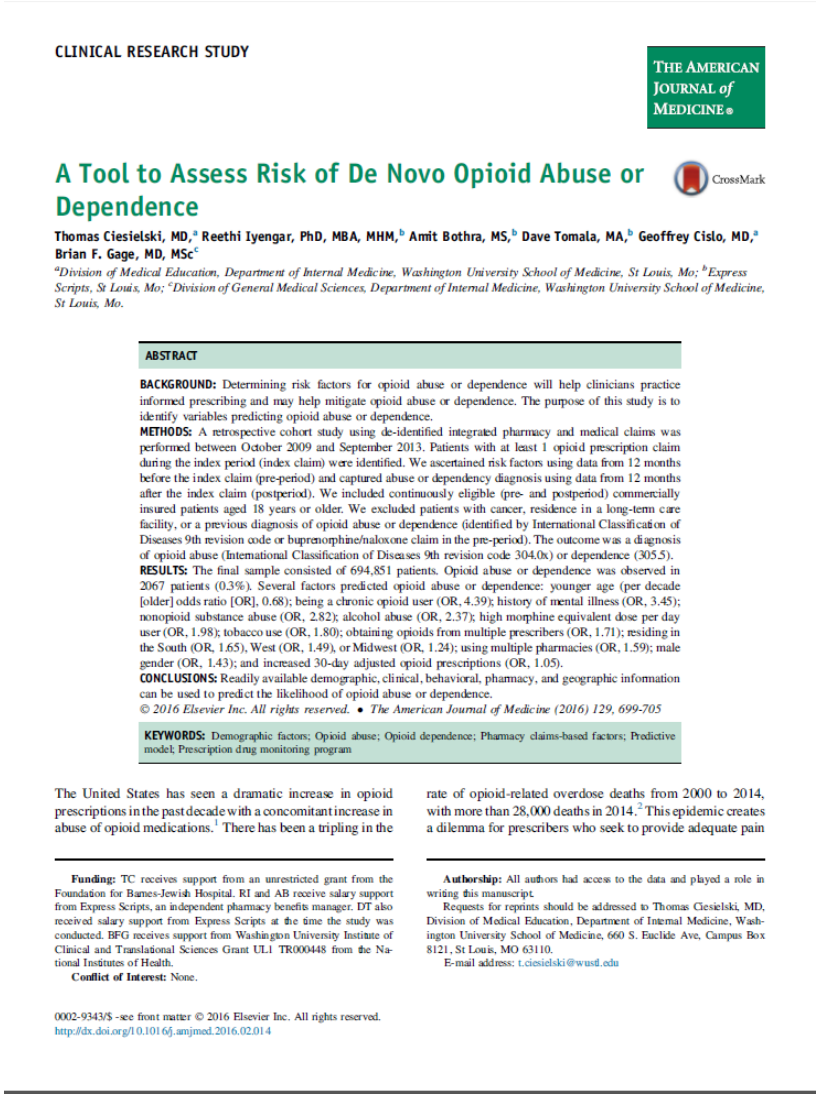
Opioid Abuse Epidemic

- There is dramatic increase in opioid prescriptions in past decade along with increase in abuse of opioid medications
  - 28,000 opioid-related overdose deaths in 2014
- One way to tackle this epidemic is to provide a way to quantify the risk of developing opioid abuse using factors readily available to physician when he is with the patient
- Express Scripts partnered with Washington University to develop a tool to predict opioid abuse and dependency which can be used by physician in their office



CLINICAL RESEARCH STUDY

THE AMERICAN JOURNAL of MEDICINE

A Tool to Assess Risk of De Novo Opioid Abuse or Dependence

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ABSTRACT

BACKGROUND: Determining risk factors for opioid abuse or dependence will help clinicians practice informed prescribing and may help mitigate opioid abuse or dependence. The purpose of this study is to identify variables predicting opioid abuse or dependence.

METHODS: A retrospective cohort study using de-identified integrated pharmacy and medical claims was performed between October 2009 and September 2013. Patients with at least 1 opioid prescription claim during the index period (index claim) were identified. We ascertained risk factors using data from 12 months before the index claim (pre-period) and captured abuse or dependency diagnosis using data from 12 months after the index claim (postperiod). We included continuously eligible (pre- and postperiod) commercially insured patients aged 18 years or older. We excluded patients with cancer, residence in a long-term care facility, or a previous diagnosis of opioid abuse or dependence (identified by International Classification of Diseases 9th revision code or buprenorphine/naloxone claim in the pre-period). The outcome was a diagnosis of opioid abuse (International Classification of Diseases 9th revision code 304.0x) or dependence (305.5).

RESULTS: The final sample consisted of 694,851 patients. Opioid abuse or dependence was observed in 2067 patients (0.3%). Several factors predicted opioid abuse or dependence: younger age (per decade [older] odds ratio [OR], 0.68); being a chronic opioid user (OR, 4.39); history of mental illness (OR, 3.45); nonopioid substance abuse (OR, 2.82); alcohol abuse (OR, 2.37); high morphine equivalent dose per day user (OR, 1.98); tobacco use (OR, 1.80); obtaining opioids from multiple prescribers (OR, 1.71); residing in the South (OR, 1.65), West (OR, 1.49), or Midwest (OR, 1.24); using multiple pharmacies (OR, 1.59); male gender (OR, 1.43); and increased 30-day adjusted opioid prescriptions (OR, 1.05).

CONCLUSIONS: Readily available demographic, clinical, behavioral, pharmacy, and geographic information can be used to predict the likelihood of opioid abuse or dependence.

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KEYWORDS: Demographic factors; Opioid abuse; Opioid dependence; Pharmacy claims-based factors; Predictive model; Prescription drug monitoring program

The United States has seen a dramatic increase in opioid prescriptions in the past decade with a concomitant increase in abuse of opioid medications.[1] There has been a tripling in the rate of opioid-related overdose deaths from 2000 to 2014, with more than 28,000 deaths in 2014.[2] This epidemic creates a dilemma for prescribers who seek to provide adequate pain

Funding: TC receives support from an unrestricted grant from the Foundation for Barnes-Jewish Hospital. RI and AB receive salary support from Express Scripts, an independent pharmacy benefits manager. DT also received salary support from Express Scripts at the time the study was conducted. BFG receives support from Washington University Institute of Clinical and Translational Sciences Grant UL1 TR000448 from the National Institutes of Health.

Conflict of Interest: None.

Authorship: All authors had access to the data and played a role in writing this manuscript.

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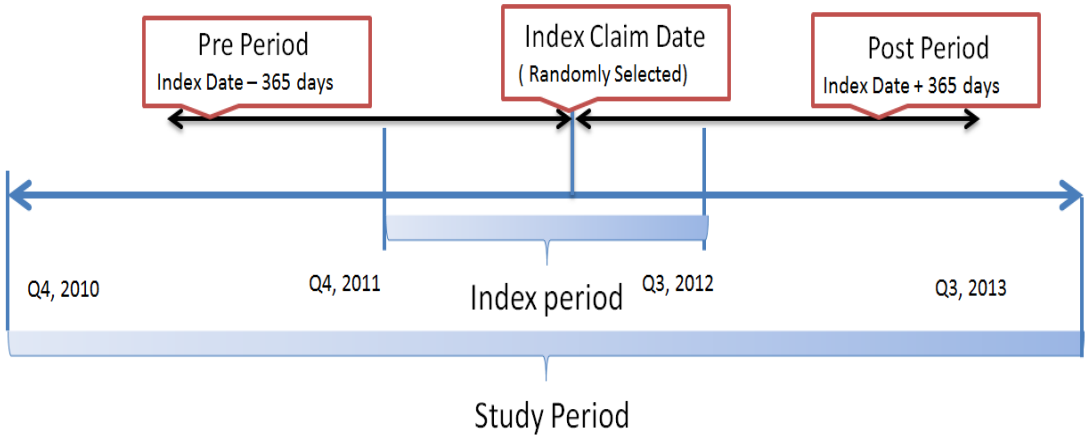
Opioid Dependency/Abuse Model

Modeling Goal	• Predict the likelihood of an opioid filling patient developing a new diagnosis of opioid Dependency or Opioid Abuse in next 12 months
Population	• Patient having at least one opioid prescription claim in the index period
Target	• The outcome was a new diagnosis of opioid abuse (ICD9 code 304.0x) or dependence (305.5).
Data Sources	• Pharmacy Rx Claims • Medical Claims
Exclusions	• Cancer Diagnosis, long-term care facilities, prior opioid dependency diagnosis, opioid antagonist(buprenorphine/naloxone), less than 18 years age

Methodology and Time Period

- Conducted a retrospective claim analysis by developing Derivation and Validation logistic regression model
  - We identified opioid filling members in 12 months index period and a opioid claim was randomly selected as index claim
  - We developed risk factors using data from 12 months prior to index claim date
  - We captured abuse or dependency diagnosis using 12 months post index claim



Note: The index period for the out-of-time validation model was Q4, 2010 to Q3 2011.

Risk Factors considered

Characteristics	Risk Factor Description
Age	Age as on index date
Gender	Patient's Gender
Non-opioid substance abuse	Patient with history of Non-opioid substance abuse in the pre-period excluding tobacco and alcohol
Tobacco use disorder	Patient with history of Tobacco abuse in the pre-period
Non-dependent alcohol abuse	Patient with history of Alcohol abuse in the pre-period
Mental Illness	Patient with history of mental illness (ICD9 codes: 290-302, 306-316) in the pre-period
Prescriber shoppers	Patient who have at least 2 prescribers for any opioid claim in 60 days pre-index date (inclusive of index date)
Pharmacy shoppers	Patient who have at least 3 pharmacies for any opioid claim in 60 days pre-index date (inclusive of index date)
Prior opioid 30-day adjusted prescriptions	Number of adjusted prescriptions for opioids in the pre-period
Chronic Users	Chronic use is defined as a patient claiming > 90 days of opioids in the six months prior to and inclusive of the index date
Opioid (MED) > 120 mg/day	Patients with >120 mg opioid dosage per day in the pre-period
Distance from patient to provider	A dichotomous flag was created with 50 mile marker based on index fill details
Chronic Immediate Release Users	Patients who were on opioids for at least 6 months of pre-period and during that time the ratio of their immediate release dosing rate is greater than 50% of their dosing rate for all opioids
Region	
Northeast	NJ, NY, PA, CT, ME, MA, NH, RI, VT
Midwest	IL, IN, MI, OH, WI, IA, KS, MN, MO, NE, ND, SD
South	DC, DE, FL, GA, MD, NC, SC, VA, WV, AL, KY, MS, TN, AR, LA, OK, TX
West	AK, CA, HI, OR, WA, AZ, CO, ID, NM, MT, UT, NV, WY

Baseline Descriptive Statistics

- Compares the demographic, behavioral, claims-based as well as geographical factors between opioid dependents and opioid non-dependents
- Statistical significance at P < 0.05 for each factor between the two groups is assessed
  - For categorical factors we use Chi-Square Test
  - For continuous factors we use T-test

- Typical SAS code:

```
/*Chi-square test for categorical
variables in the final model*/

proc freq data = two;

  tables gender*OUTCOME_OR_TARGET /
chisq;

run;

/*t-test for continuous variables in
the final model*/

proc ttest data = two;

  class OUTCOME_OR_TARGET;

  var age;

run;
```

Predictive Model Development

- Multivariate Logistic regression was performed to predict the likelihood of opioid abuse or dependence
  - Entire data and all the factors were used to build the model
- Validation was conducted to assess performance of the predictive model in an independent sample
- For categorical variables we use the class option
  - Use ref option to identify the reference class for each variable

```
proc LOGISTIC data=model_data;
class distance_recoded2_sas (ref = '0')  non_opioid_pre_period (ref='0')
      alcohol_use_pre_period (ref = '0') tobacco_use_pre_period (ref = '0')
      gender (ref = '1')                 mental_illness_pre_period (ref = '0')
      med_120 (ref = '0')                cont_90_days_pre_period (ref = '0')
      irmorethanhalf_12 (ref = '0')      at_least_2_provider (ref = '0')
      atleast_3_phar (ref = '0')         region_combined (ref = 'NORTHEAST_COMBINED')
  / param=ref;
model OUTCOME_OR_TARGET (event = '1') = age_dec                opioid_Adj_rx_pre_period
                                        gender                 non_opioid_pre_period
                                        tobacco_use_pre_period alcohol_use_pre_period
                                        med_120                mental_illness_pre_period
                                        region_combined        cont_90_days_pre_period
                                        irmorethanhalf_12      at_least_2_provider
                                        atleast_3_phar         distance_recoded2_sas
                                        / rsq ;

run;
```

Sensitivity Analysis for Rare target

- Only 0.3% of the patients were diagnosed as Opioid abusers or dependent
- To address potential bias in the estimated coefficient resulting from the rare target and to test the robustness of the findings, 2 sensitivity analyses were conducted
  - Firth penalized maximum Likelihood Method
  - Over Sampling
- We oversample the target 10 times to increase target rate from 0.3 to 3%
- Sensitivity analysis result were consistent with main findings

```
• /*Firth Estimation Method*/
proc Logistics data = model_data;
Class … … /param =ref;
model OUTCOME_OR_TARGET (event = '1') =
 age gender …… / firth;
run;
• /* Oversampling. Made the target
rate 3% from 0.3%*/
data event nonevent;
set model_data;
if OUTCOME_OR_TARGET then output event;
else output nonevent;
run;
PROC SURVEYSELECT DATA=WORK.NONEVENT()
OUT=WORK.RANDNONEVENT
METHOD=SRS N=66900 SEED=369106935;
RUN;
```

Results

	Reference	Derivation Model[c]		Validation Model[c]	
		OR[a]	95% CI	OR[a]	95% CI
Age (per decade of life)	NA	0.68	[0.65,0.70]	0.65	[0.63,0.68]
Gender	Female	1.43	[1.31,1.57]	1.52	[1.37,1.68]
Non-opioid substance abuse	No	2.82	[2.18,3.64]	2.87	[2.11,3.89]
Tobacco use disorder	No	1.80	[1.60,2.04]	2.09	[1.81,2.40]
Non-dependent alcohol abuse	No	2.37	[1.84,3.05]	2.10	[1.55,2.85]
Mental illness	No	3.45	[3.13,3.79]	3.37	[3.02,3.76]
Prescriber shoppers	No	1.71	[1.55,1.89]	1.74	[1.55,1.95]
Pharmacy shoppers	No	1.59	[1.31,1.92]	1.98	[1.61,2.43]
Prior opioid 30-day adjusted prescriptions	NA	1.05	[1.04,1.06]	1.04	[1.03,1.05]
Chronic users	No	4.39	[3.71,5.19]	4.29	[3.53,5.22]
Daily MED > 120 mg/day	No	1.98	[1.68,2.34]	1.93	[1.61,2.32]
Chronic, immediate release user	No	1.07[b]	[0.93,1.22]	1.27	[1.09,1.48]
Distance from patient to prescriber	≤50 miles	1.12[b]	[0.99,1.27]	0.95[b]	[0.83,1.10]
Region					
Midwest	Northeast	1.24	[1.08,1.42]	1.31	[1.13,1.53]
South	Northeast	1.65	[1.45,1.87]	1.44	[1.25,1.67]
West	Northeast	1.49	[1.29,1.72]	1.70	[1.46,1.99]

[a] All data were significant at P<0.05 unless marked with a note indicating otherwise
[b] Not significant at P<0.05
[c] The c-statistics were 0.852 for the derivation model and 0.847 for the validation model.
NA: Not applicable for continuous variables
MED: Morphine equivalent dose

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Thank You