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Characterization of Potentially Unsafe Prescribing of Opioid Analgesics Requiring Prior Opioid Tolerance (OTOs)

Joint meeting of the Drug Safety and Risk Management Advisory Committee and the Anesthetic and Analgesic Drug Products Advisory Committee, August 3, 2018

Molly Moore Jeffery, PhD
Scientific Director of Emergency Medicine Research
Research Associate, Department of Health Sciences Research
Mayo Clinic

Acknowledgments

OptumLabs

Christine Chaisson
Christopher Hane
Louis Rumanes
Darshak Sanghavi
Aylin Altan
Jamie Tucker
Lillian Hang
Jane Sullivan
Pamela Hansen

Yale-Mayo Clinic CERSI

Molly Jeffery
Nilay Shah
Rozalina McCoy
W. Michael Hooten
Hongfang Liu
Joseph Ross

FDA

Judy Staffa
Judith Racoosin
Catherine Dormitzer
Cynthia Kornegay
Audrey Thomas
Rebekah Zinn

This study was supported by a Center of Excellence in Regulatory Science and Innovation (CERSI) grant to Yale University and Mayo Clinic from the US Food & Drug Administration (U01FD005938). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the HHS or FDA.

STUDY: Characterization and Analysis of Incidence of Potentially Unsafe Prescribing of Certain Opioid Analgesics Requiring Prior Tolerance Using Natural Language Processing (NLP) of Electronic Health Record (EHR) Clinical Notes



Aim 1

Use claims data to determine the frequency of prescribing of opioid-tolerant-only (OTO) drugs to patients who do not appear to have evidence of opioid tolerance at the time of prescribing.

Aim 2

Use structured fields in the EHR (phase 1) and NLP techniques to extract information from clinical notes (phase 2) to determine whether information from EHR identifies opioid tolerance beyond that found in claims data. These efforts will verify or challenge the preliminary findings of the claims based algorithms.

Data Sources

Aim 1: claims from OptumLabs Data Warehouse (commercial and Medicare Advantage)

- Enrollment Data
- Physician Claims
- Facility Claims
- Pharmacy Claims

Aim 2: electronic health record data from OptumLabs Data Warehouse (all payer types) and free-text notes

- Structured data
 - Hospitalization
 - Outpatient
 - Prescriptions written
- Clinical notes

Definitions of Opioids Requiring Prior Tolerance

- Extended-release (ER) oxycodone defined as a cumulative daily dose >80mg, or drug strength of 60 or 80 mg
- Extended-release hydromorphone at any dose
- Transdermal fentanyl at any dose
- Transmucosal immediate release fentanyl (TIRF) at any dose

Definition of Opioid Tolerance

From Larochelle et al. 2017*

Tolerance 1	Evidence of ≥ 30 mg of oxycodone equivalents on each day of the 7 days prior to OTO episode, exclusive of start date
Tolerance 2	Evidence of at least 7 days of ≥ 30 mg of oxycodone equivalents in the 30 days prior to OTO episode, exclusive of start date. The seven days are not required to be consecutive
Tolerance 3	Evidence of > 0 mg of oxycodone equivalents on each of the 7 days prior OTO episode, exclusive of start date
Tolerance 4	Evidence of at least 7 days of > 0 mg oxycodone equivalents in the 30 days prior to the OTO episode, exclusive of start date. The seven days are not required to be consecutive

Aim 1- Claims Data

Inclusion criteria: claims study

- 6 months continuous enrollment with both pharmacy and medical benefits (commercial or Medicare Advantage)
- Evidence of an opioid-tolerant-only (OTO) prescription between January 1, 2007 to December 31, 2016
- No OTO prescription in the prior 183 days
- No opioid poisoning/overdose diagnosis in prior 183 days
- No hospitalization in prior 30 days

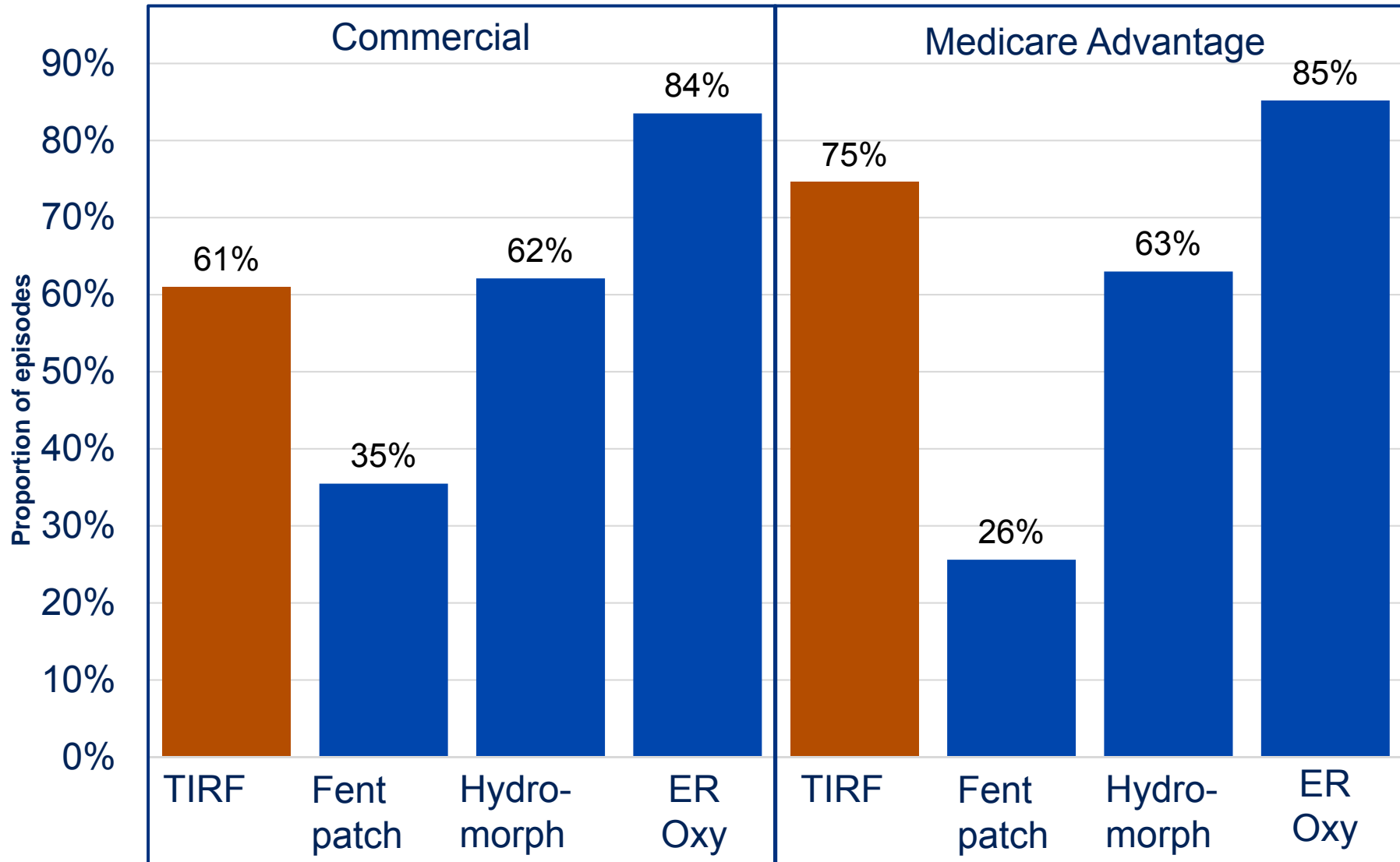
153,385 OTO episodes contributed by 131,756 individuals

41% of episodes Medicare Advantage

Fentanyl patch most common (66%)

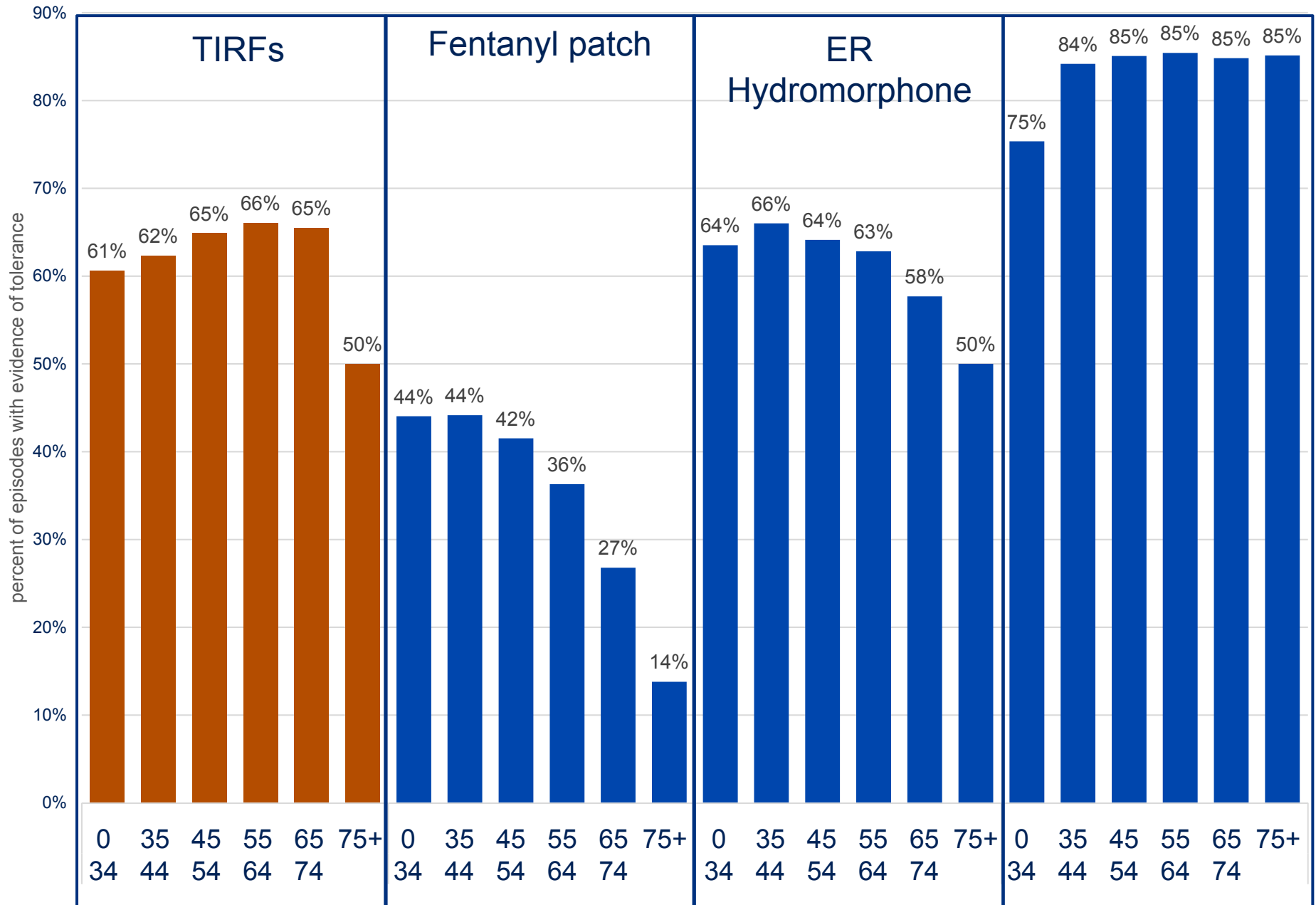
2,440 TIRF episodes

Tolerant when starting OTO episode

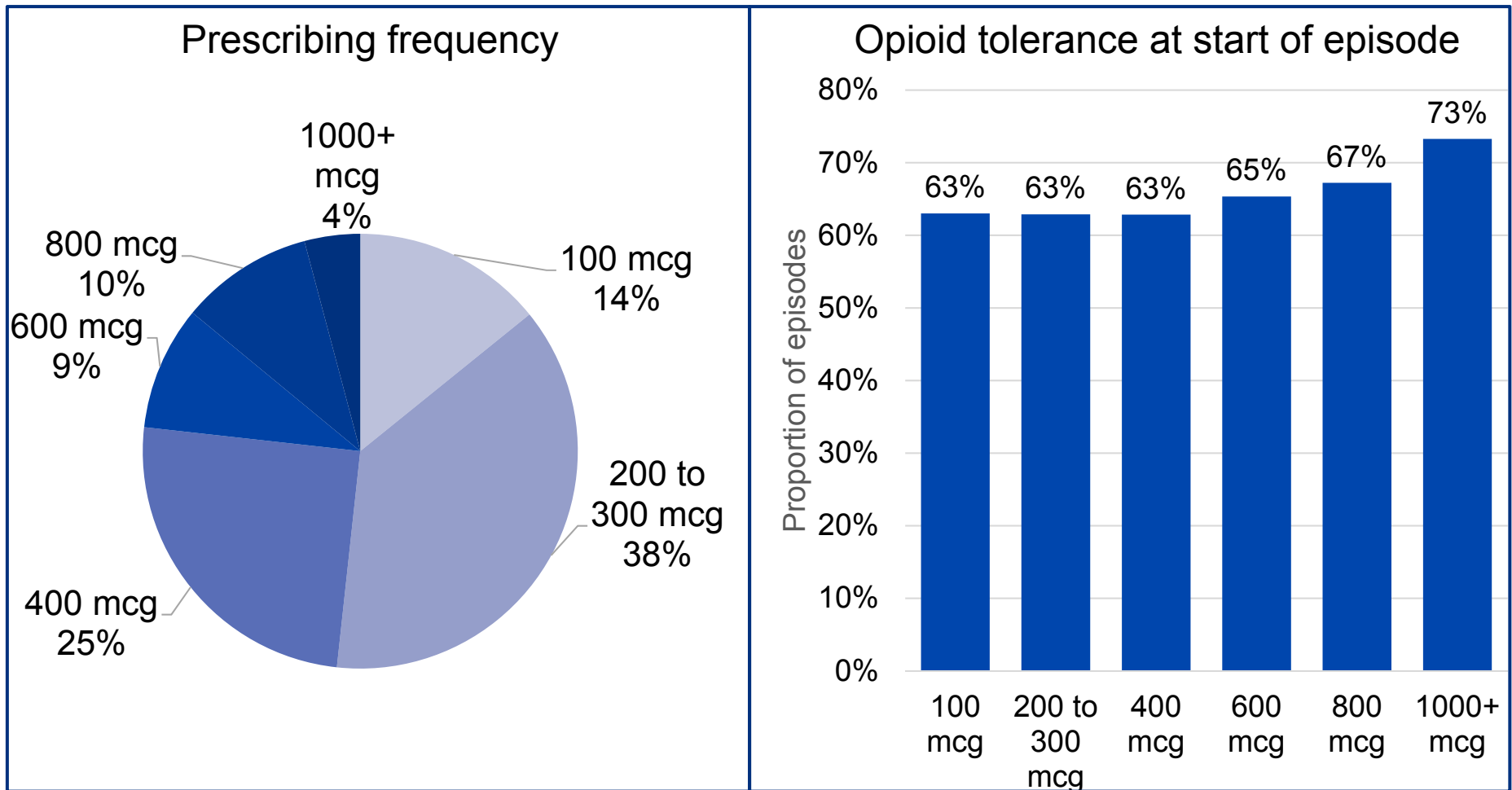


Tolerance by age group

ER Oxycodone



TIRF episodes: strength of initial prescription



Aim 1 Summary

- More 150,000 OTO episodes studied, including 2400 TIRF episodes
- Highest rates of tolerance in ER oxycodone (84%); lowest rates in fentanyl patches (31%)
- TIRF episodes: 61% of commercially insured, 75% of Medicare Advantage demonstrated primary opioid tolerance
- Tolerance similar across TIRF doses <1000 mcg

Aim 2 – Electronic Health Record (EHR) Data

Electronic Health Record (EHR) and Notes Data

Electronic Health Record:

- Derived from dozens of healthcare provider organizations in US: 700 Hospitals, 7,500 Clinics, treating >64 million patients
- Includes all insurance types as well as uninsured
- There is no “continuous enrollment” concept in an EHR environment
 - “Leakage” is a salient issue: absence of an event doesn’t mean it didn’t happen

Types of notes:

- Outpatient Office Visits
- Consultation Reports
- Operative (Procedure) Reports
- Admission, Discharge Summaries
- Nursing
- Labs
- Emergency Department
- Pathology
- Radiology
- Cardiology
- Etc.

Electronic Health Record (EHR) study

Inclusion criteria

- Identified OTO episode in claims analysis
- EHR activity within 183 days of claims OTO

Approach

- Compare evidence of opioid tolerance in **claims** to evidence in **EHR**

20,044 OTO episodes matched between claims and EHR

PLUS 46,525 OTO episodes with notes used for textual analysis

249 OTO episodes matched between claims and notes sample

Not enough TIRF episodes to analyze separately

Similar distribution of OTO drugs vs. claims

Does EHR data enhance evidence of tolerance for OTO prescriptions found in claims?

Evidence of Primary Tolerance for OTO Episodes in Claims and EHR		
Evidence of tolerance identified in Claims		
	Yes	No
Evidence of tolerance identified in Structured EHR Data	Yes A. Agree	No B. Enhance
	No C. Refute/ Missing Data	D. Agree/ Missing Data

Additional information found in EHR structured data

Evidence of Primary Tolerance for OTO Episodes in Claims and EHR				
		Evidence of Tolerance in Claims		
		Yes	No	Total
Evidence of Tolerance in Structured EHR	Yes	520 (2.5%)	108 (0.5%)	628 (3.1%)
	No	8,725 (43.5%)	10,691 (53.3%)	19,416 (96.9%)
	Total	9,245 (46%)	10,799 (54%)	20,044

Textual analysis of notes

- Used NLP to summarize notes into **topics**
- Identified hundreds of important **terms**
- Tested whether **topics** or **terms** could be identified that differentiated between people who did and did not have evidence of tolerance in claims data

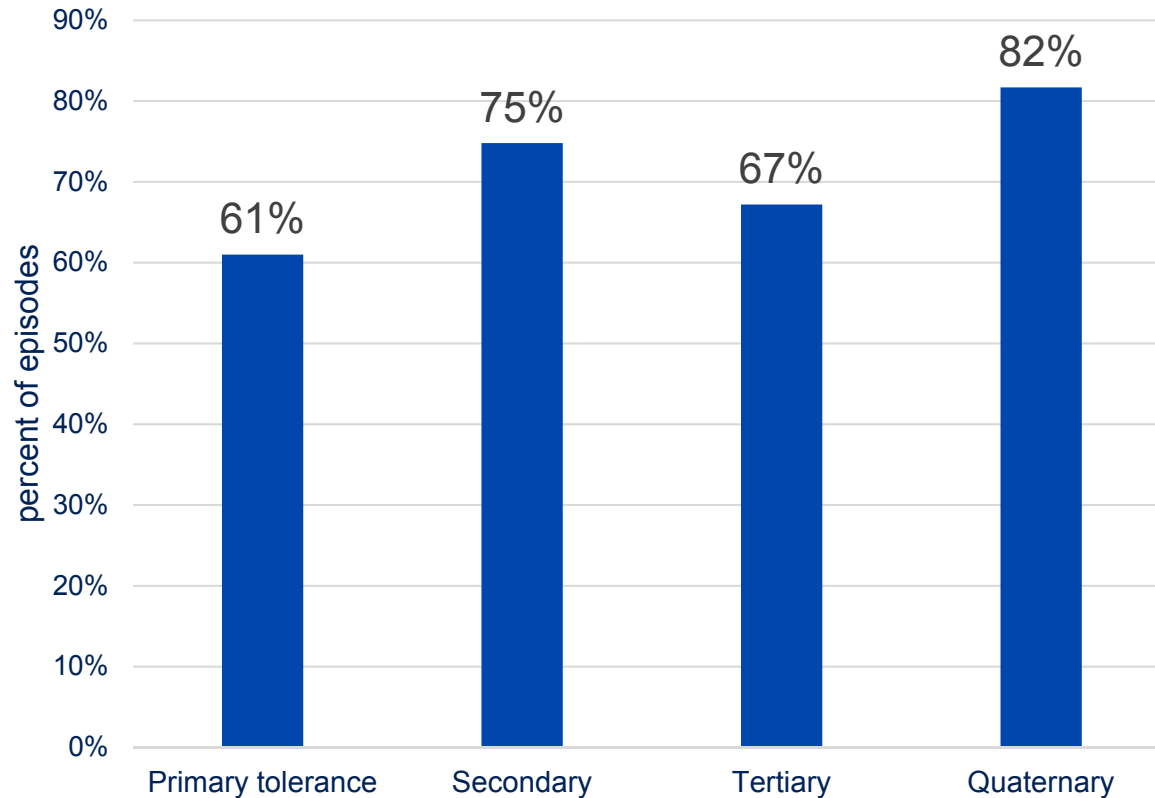
High level result: no terms or topics associated with missing evidence of tolerance in claims data

Summary

- Studies using claims data have found many ($\sim 1/2$) prescriptions for opioids requiring prior tolerance do not have any evidence of prior tolerance
- Adding electronic health record (EHR) data – from structured fields or using NLP against patient notes – provides a minimal amount of additional evidence of appropriate opioid prescribing (prior tolerance)
- Based on our extensive exploration of EHR data, we believe results of our and prior claims analysis to be generally accurate
- We did not evaluate the implications of the apparently inappropriate prescribing or whether patients suffered any harm as a result of these inappropriate prescriptions

Backup Slides Shown

Other tolerance definitions: TIRFs



Primary: ≥ 30 mg oxycodone equivalent dose in 7 days prior

Secondary: ≥ 30 mg oxycodone equivalent dose in 7 out of 30 days prior

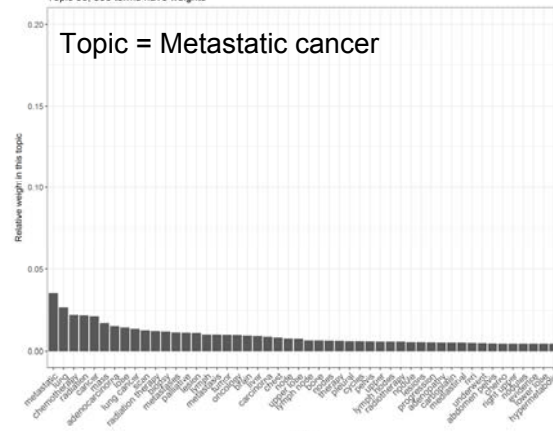
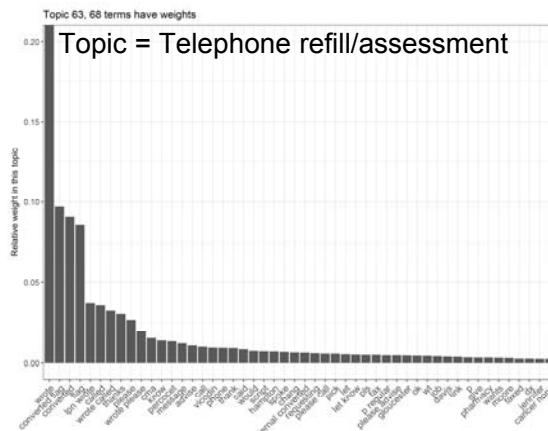
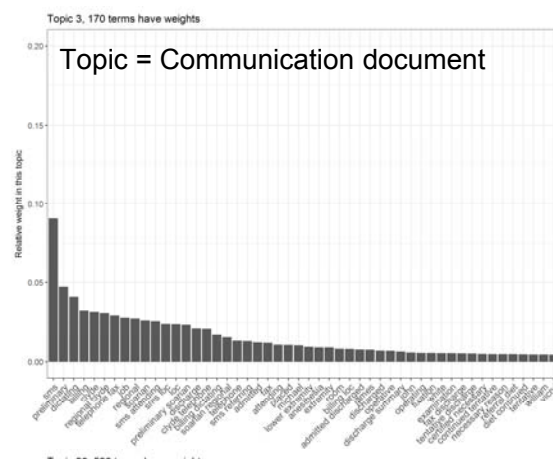
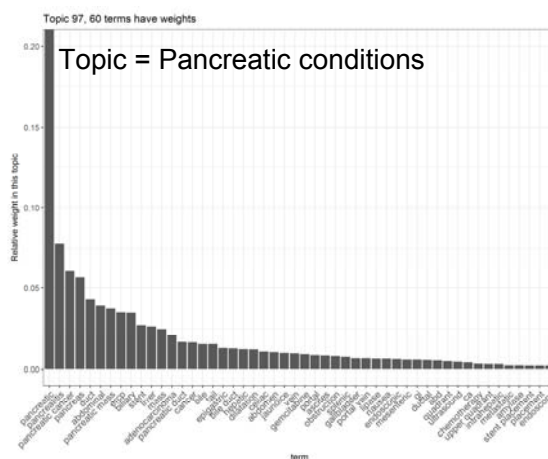
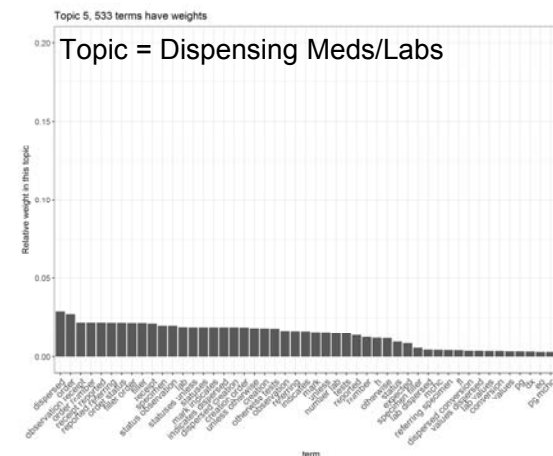
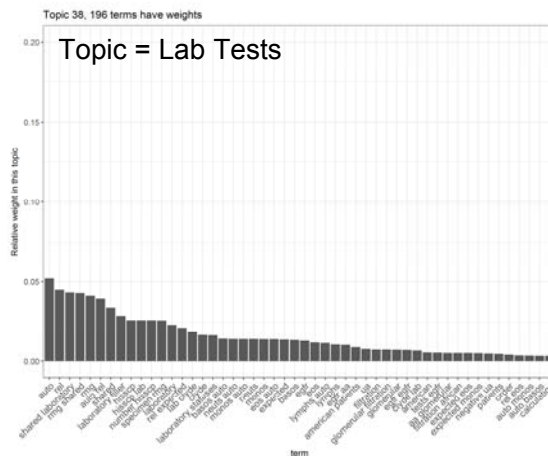
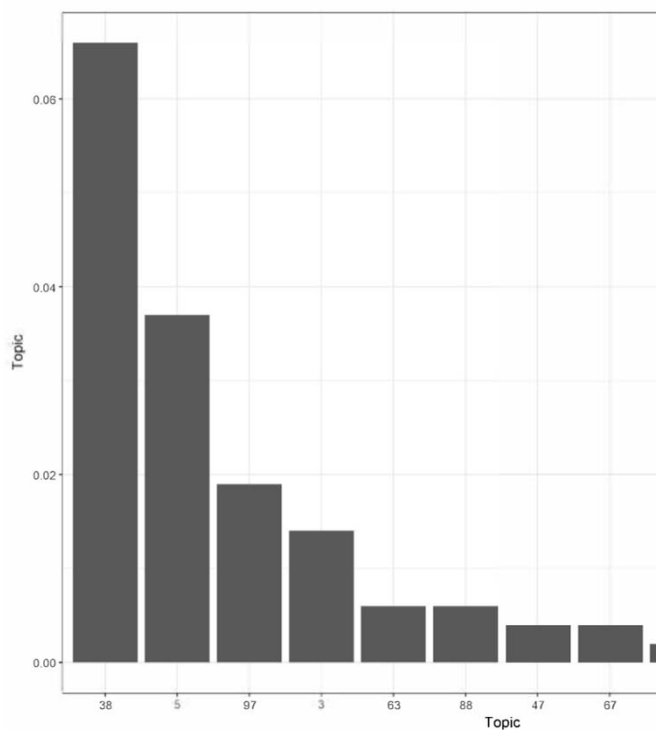
Tertiary: > 0 mg oxycodone equivalent dose in 7 days prior

Quaternary: > 0 mg oxycodone equivalent dose in 7 out of 30 days prior

Comparison of Evidence of Tolerance when OTO identified in claims or in both claims and EHR

OTO defined by Claims only					
Evidence of Tolerance for OTO Episodes					
in Claims					
		Yes	No	Total	
in Structured EHR	Yes	520 (2.5%)	108 (0.5%)	628 (3.1%)	
	No	8,725 (43.5%)	10,691 (53.3%)	19,416 (96.9%)	
	Total	9,245 (46%)	10,799 (54%)	20,044	
OTO defined in Claims + EHR Rx within +/- 14 days					
Evidence of Tolerance for OTO Episodes					
in Claims					
		Yes	No	Total	
in Structured EHR	Yes	271 (29%)	40 (4%)	311 (33%)	
	No	120 (13%)	508 (54%)	628 (67%)	
	Total	391 (42%)	548 (58%)	939	

Example Note summary



Topic 97, 60 terms have weights

