Estimating "Optimal" Durations for Initial Opioid Analgesic Prescription Following Common Surgical Procedures

International Conference on Pharmacoepidemiology & Therapeutic Risk Management (34th ICPE)

August 25, 2018

Justin Bohn, Sc.D., Harvard Pilgrim Health Care Institute

On behalf of
***Mallika Mundkur, M.D., M.P.H.,** U.S. Food and Drug Administration*

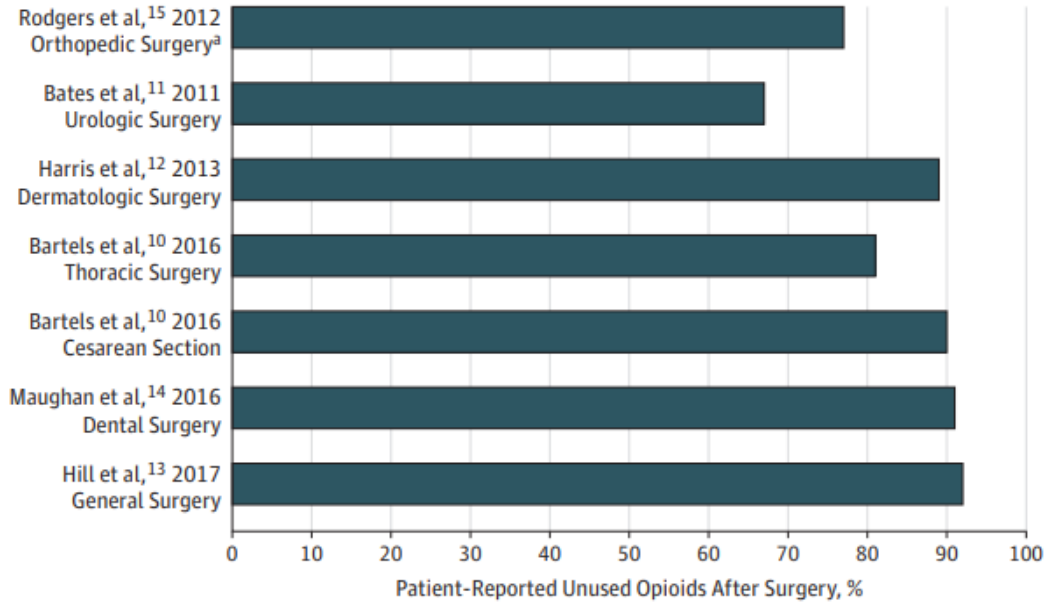
Disclosures

- The authors have no conflicts of interest to disclose
- This work was co-led by FDA partners and supported by FDA through the Department of Health and Human Services (HHS) Contract number HHSF223201400030I
- This presentation reflects the views of the authors and not necessarily those of the U.S. FDA

Excess opioid prescribing after surgery

- Patients report excess opioid analgesics (OAs) after surgery[1-3]
  - Leftover supply affords opportunity for unintended use, misuse, abuse, overdose or diversion
  - Can "refilling" behavior in claims inform appropriate dispensing?

Figure. Prevalence of Unused Opioids Prescribed After Surgery



[1] *Bicket et al. JAMA Surg. 2017 Nov 1;152(11):1066-1071.*
[2] *Hill et al. Ann Surg. 2017 Apr;265(4):709-714.*
[3] *Hill et al. J Am Coll Surg. 2018 Jun;226(6):996-1003..*

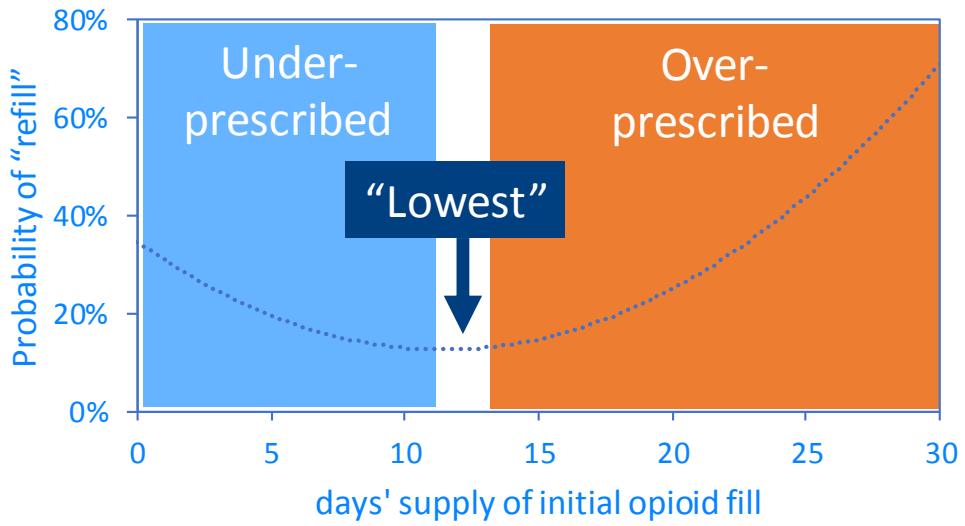
One approach to assessing "refill" behavior

JAMA Surgery | Original Investigation

Defining Optimal Length of Opioid Pain Medication Prescription After Common Surgical Procedures

Rebecca E. Scully, MD; Andrew J. Schoenfeld, MD, MSc; Wei Jiang, MS; Stuart Lipsitz, ScD; Muhammad Ali Chaudhary, MBBS; Peter A. Learn, MD; Tracey Koehlmoos, PhD, MHA; Adil H. Haider, MD, MPH; Louis L. Nguyen, MD, MBA, MPH

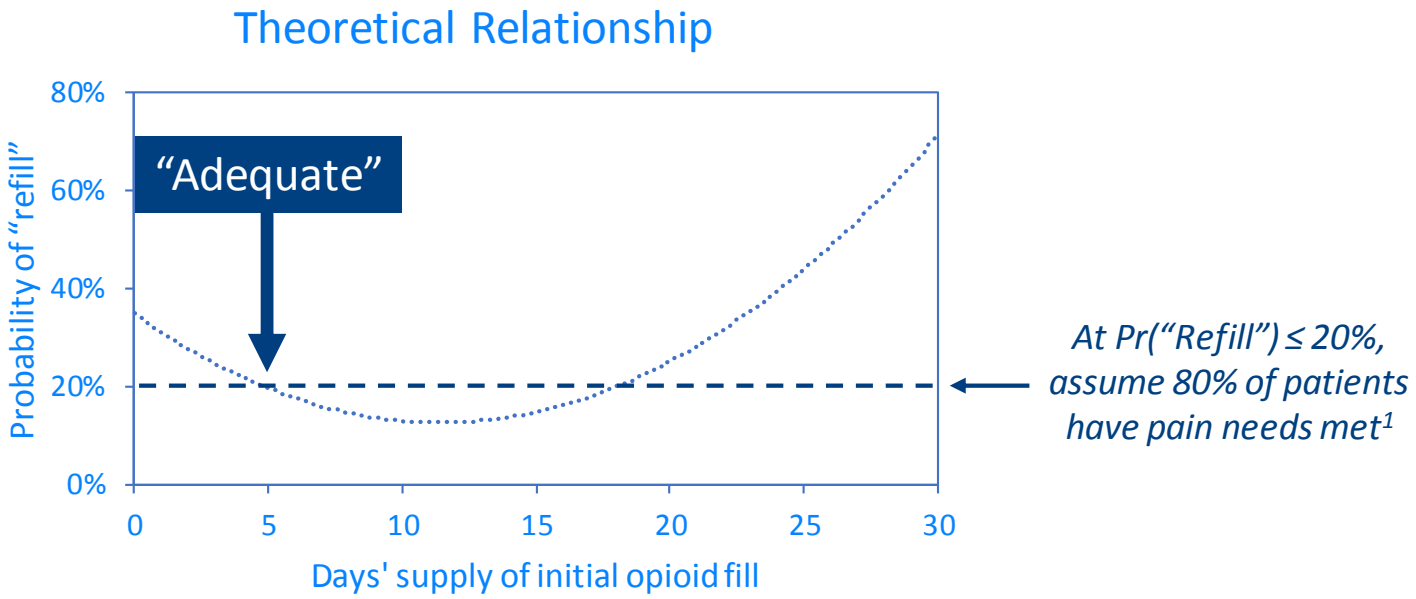
Theoretical Relationship



Scully Method

1. Identify post-op opioid initiators
   Follow for subsequent "refill"
2. Fit model for probability of refill
   Include terms for flexible function of days' supply + confounders
3. Plot adjusted relationship
   Nadir of curve used to estimate length of initial prescription associated with lowest refill rate

Another approach



- Identify first days' supply at which 20% or fewer "refill"
- Absolute cutoff reflects clinical recommendations

[1] *Hill et al. An Educational Intervention Decreases Opioid Prescribing After General Surgical Operations. Ann Surg. 2018 Mar;267(3):468-472*

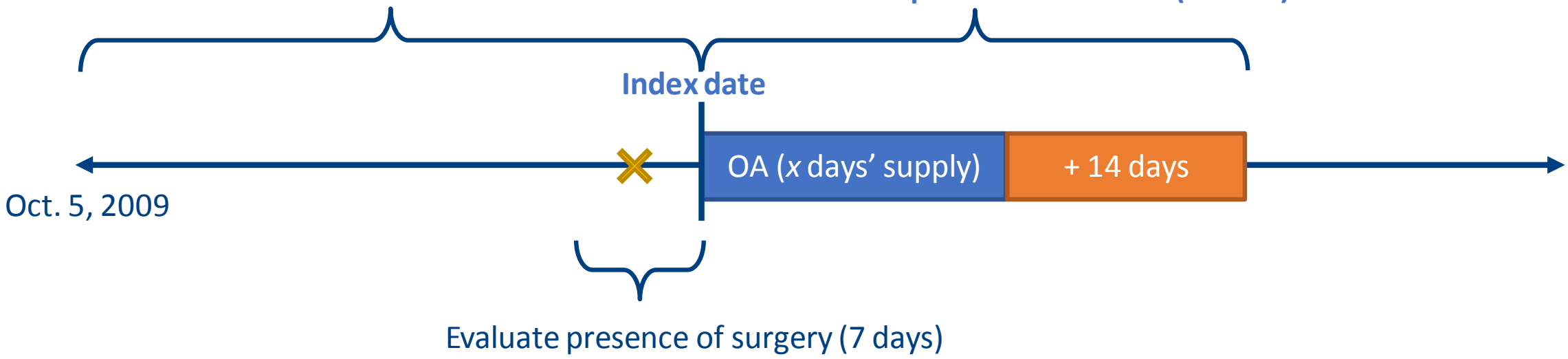
Study overview

- Data source
  - Sentinel Distributed Database
  - Claims from 17 Data Partners
- Study period
  - October 5, 2009 to October 5, 2014
- Exposure
  - Index event: Opioid dispensing ≤ 30 days' supply
- Outcome
  - "Refill" – a second dispensing of *opioid within 14 days of the end of supply of index dispensing*
- Inclusions
  - One of 11 surgical procedures in 7 days before index
  - Continuous enrollment for 183 days before and 45 days after index
- Exclusions
  - Prior opioid dispensing
  - Prior surgery
  - Prior substance abuse disorder diagnosis
  - Prior cancer

Study design

Evaluate exclusions (183 days)

- OA dispensing
- Other study surgery
- Substance abuse disorder diagnosis
- Cancer diagnosis



Surgeries of interest*

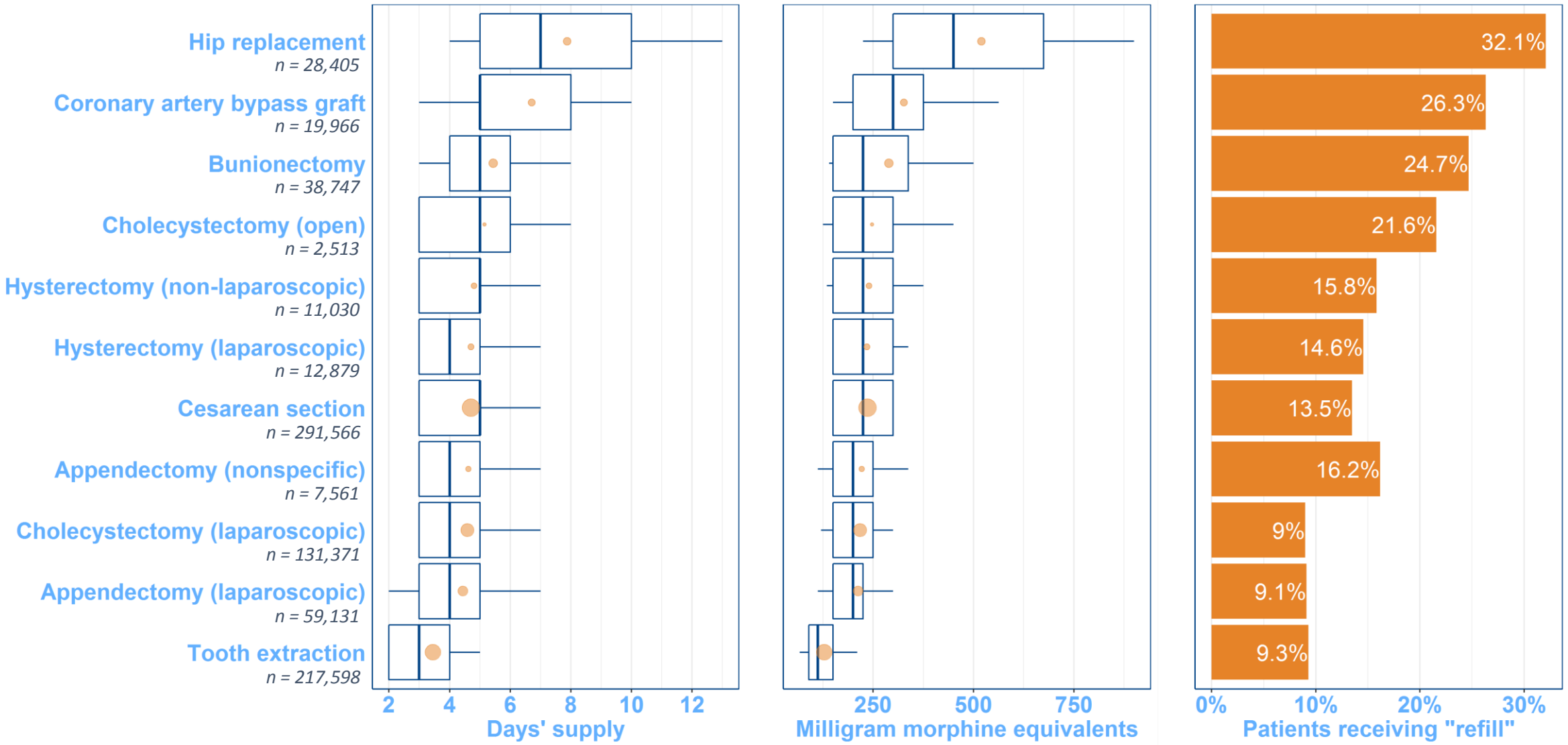
- Appendectomy
  - *Laparoscopic*
  - *Nonspecific*
- Bunionectomy
- Cesarean section
- Cholecystectomy
  - *Open*
  - *Laparoscopic*
- Coronary artery bypass graft
- Hip replacement
- Hysterectomy
  - *Non-laparoscopic*
  - *Laparoscopic*
- Tooth extraction
- Not presented
  - Hip fracture treatment
  - Knee arthroplasty
  - Laminectomy/discectomy
  - Spinal fusion

* Selected based on frequency in Healthcare Cost and Utilization Project (HCUP) data

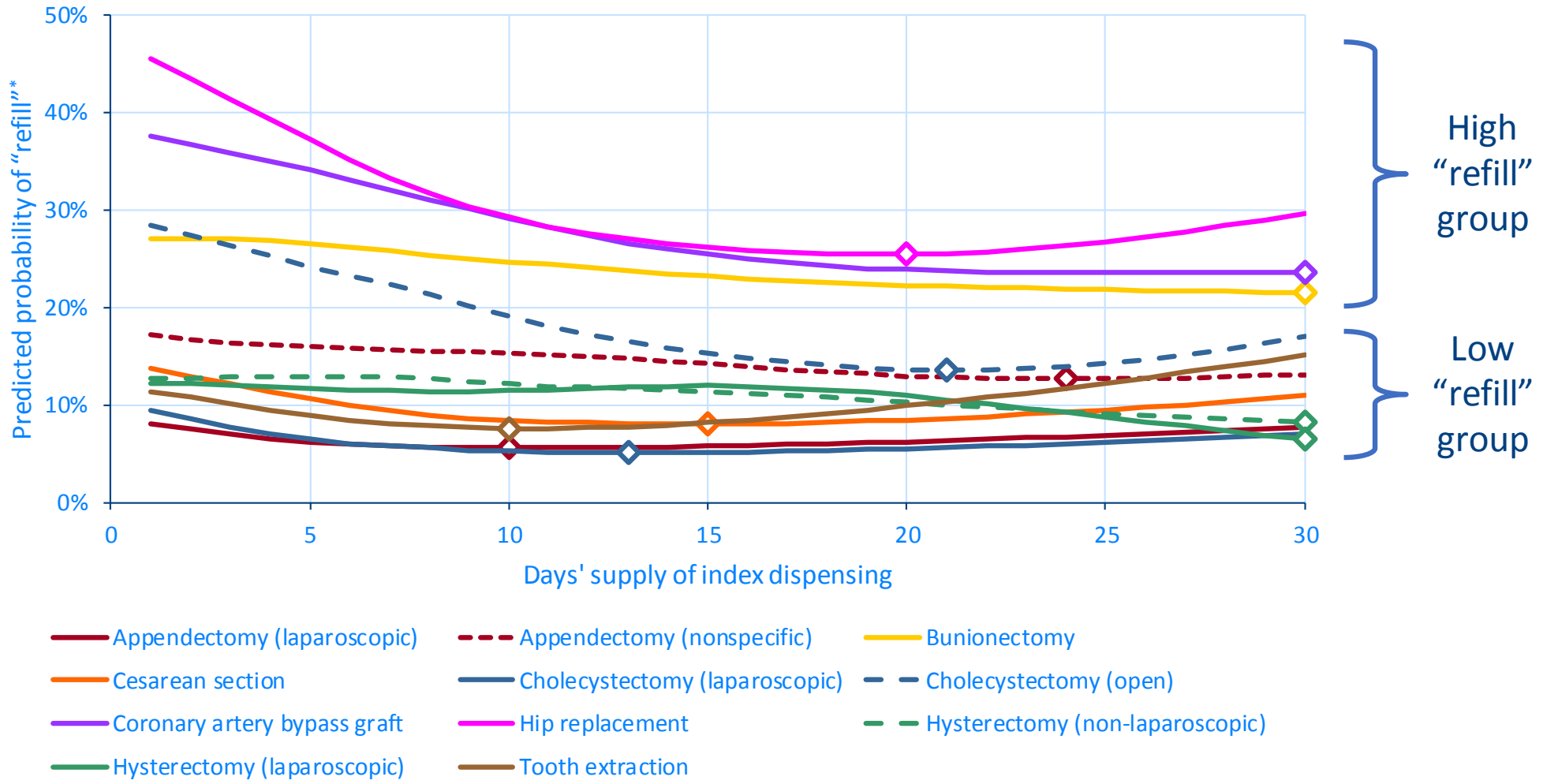
Analytic plan

- Characterize post-surgical OA initiators
  - Demographics
  - Opioid received (active moiety, amount, Drug Enforcement Agency (DEA) schedule, etc.)
  - Presence and time to “refill”
- Fit generalized additive logistic model for probability of “refill”
  - Smooth spline function of days’ supply
  - Adjust for age, sex, year, Charlson-Elixhauser Combined Comorbidity Index, DEA schedule, Data Partner
- Describe adjusted relationship between days’ supply and probability of “refill”
  - Identify “lowest” and “adequate” cutoffs for each surgery

Observed quantities dispensed



Modeled results in our study



*Predictions refer to a hypothetical female reference patient aged 18-64 years, with a combined comorbidity score < 1, initiating a schedule II opioid in 2014 at a large reference Data Partner

Our results and comparison

	Patients	Observed days' supply	Modeled days' supply		
		Median (IQR)	"Adequate"	Sentinel "Lowest" (% "Refill")	Scully "Lowest" (% "Refill")
Appendectomy					
Laparoscopic	59,131	4 (2)	1	10 (5.6%)	9 (11%)
Nonspecific	7,561	4 (2)	1	24 (12.7%)	
Bunionectomy	38,747	5 (2)	*	30 (21.6%)	N/A
Cesarean section	291,566	5 (2)	1	15 (8.0%)	N/A
Cholecystectomy					
Laparoscopic	131,371	4 (2)	1	13 (5.1%)	9 (11%)
Open	2,513	5 (3)	10	21 (13.5%)	
Coronary artery bypass graft	19,966	5 (3)	*	30 (23.7%)	N/A
Hip replacement	28,405	7 (5)	*	20 (25.5%)	N/A
Hysterectomy					
Non-laparoscopic	11,030	5 (2)	1	30 (8.2%)	13 (17%)
Laparoscopic	12,879	4 (2)	1	30 (6.5%)	
Tooth extraction	217,598	3 (2)	1	10 (7.6%)	N/A

"lowest" : value with lowest "refill" probability
"adequate": first value with "refill" probability ≤ 20%
**modeled probability of refill always exceeds 20%*

Limitations

- No information on *actual pain levels* of patients
- Strong assumptions about “refilling” behavior
  - How strong is correlation with inadequate pain management?
- Predictions refer to potentially non-representative “reference patient”
- Limited coverage of elderly population
- Potential issues identifying surgery dates
  - Specifically for backdated inpatient procedures, is OA dispensed after > 7 days?

Conclusions

- Prescriptions of <7 days already common for many surgeries
- Substantial between-surgery variation
  - Initial duration dispensed & likelihood of “refilling”
- Replication of Scully et al. in representative population
  - Distribution of initial duration
  - Overall “refill” probability
  - Characteristic “U”-shaped curve
- “Lowest” duration method suggests longer initial prescribing durations than is currently practiced
- “Adequate” duration method suggests often single day is enough for many procedures

Next steps

- Addition of new populations
  - Center for Medicare and Medicaid services
  - Pediatric populations
- Denominator information
  - What % of surgical patients receive an opioid?
- Lowest/adequate cutoffs for number of tablets/capsules, morphine milligram equivalents (MMEs)
- Marginal, population-level predictions
- Importance of predictors of “refill”
  - Is surgery type a more important predictor of “refilling” than days supplied?
  - What about comorbidity, gender, Data Partner, etc.?

Acknowledgements

US Food and Drug Administration

- Co-authors
  - Mallika Mundkur, MD, MPH
  - Tamra Meyer, PhD, MPH
  - Joan Xie, PhD
  - David Graham, MD, MPH
  - Judy Staffa, PhD, RPh

Sentinel Operations Center

- Co-authors
  - Talia Menzin, BS
  - Judy Maro, PhD
- Additional support
  - Tiffany Woodworth, MPH, MBA
  - Darren Toh, ScD
  - Zilu Zhang, MS

Many thanks are due to Data Partners who provided data used in the analysis