# Evaluation of Switching Patterns in FDA's Sentinel System – A New Tool to Assess the Substitutability of Generic Drugs

Sarah K. Dutcher,[1] Jennifer R. Popovic[2,3] Michael Nguyen,[1] Sukhminder K. Sandhu,[1] Patty Greene,[1] Rima Izem,[1] Wenlei Jiang,[1] Zhong Wang,[1] Yueqin Zhao,[1] Andrew B. Petrone,[2] Anita K. Wagner,[2] Joshua J. Gagne[4]

1. Center for Drug Evaluation and Research, US Food and Drug Administration, Silver Spring, MD
2. Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA
3. RTI International, Waltham, MA
4. Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA

# Disclosures

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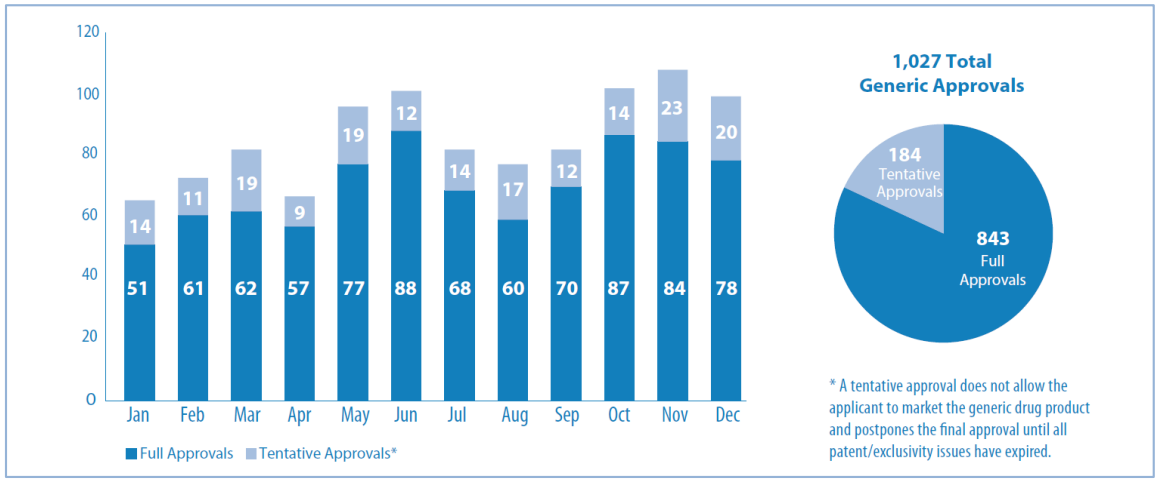
# Generic Drugs

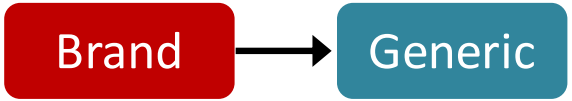
- Most drugs dispensed in the U.S. (90%) are generic products[1]
- FDA's Office of Generic Drugs (OGD) approved 1,027 generic drugs in 2017[2]



# Generic Drug Substitutability

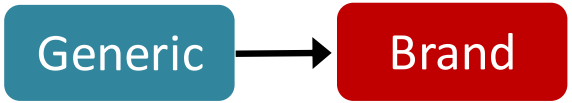
- Over the past decade, several observational studies have been published that question the bioequivalence of generic drugs[3-6]
- From 2011-2016, OGD took regulatory action on three products related to issues of therapeutic inequivalence[7-9]
- In 2017, OGD received ~640 individual spontaneous case reports related to the quality of generic drugs each month
  - 55% described issues related to switching between brand and generic

# Generic Drug Substitutability




Why switch?

- Insurance formulary
- Lower patient costs (e.g., copays)
- State generic substitution laws (permissive or mandatory)
- Drug availability




Why switchback?

- Patient experiences effectiveness or safety issue
- Patient preference
- Physician preference (“Dispense as written”)

# Objective

- Existing Sentinel tools were limited in their ability to study brand and generic switching patterns
- **To develop and implement a modular, reusable tool for describing manufacturer-level drug utilization and switching patterns in the US FDA's Sentinel System**

# Data Source: Sentinel

- FDA's active surveillance system for medical products
- Uses electronic healthcare data from a distributed data network of 18 Data Partners formatted into a common data model
- For tool testing, data from the 4 largest Data Partners in Sentinel were used
  - National health insurers
  - Comprise 88% of total patient data

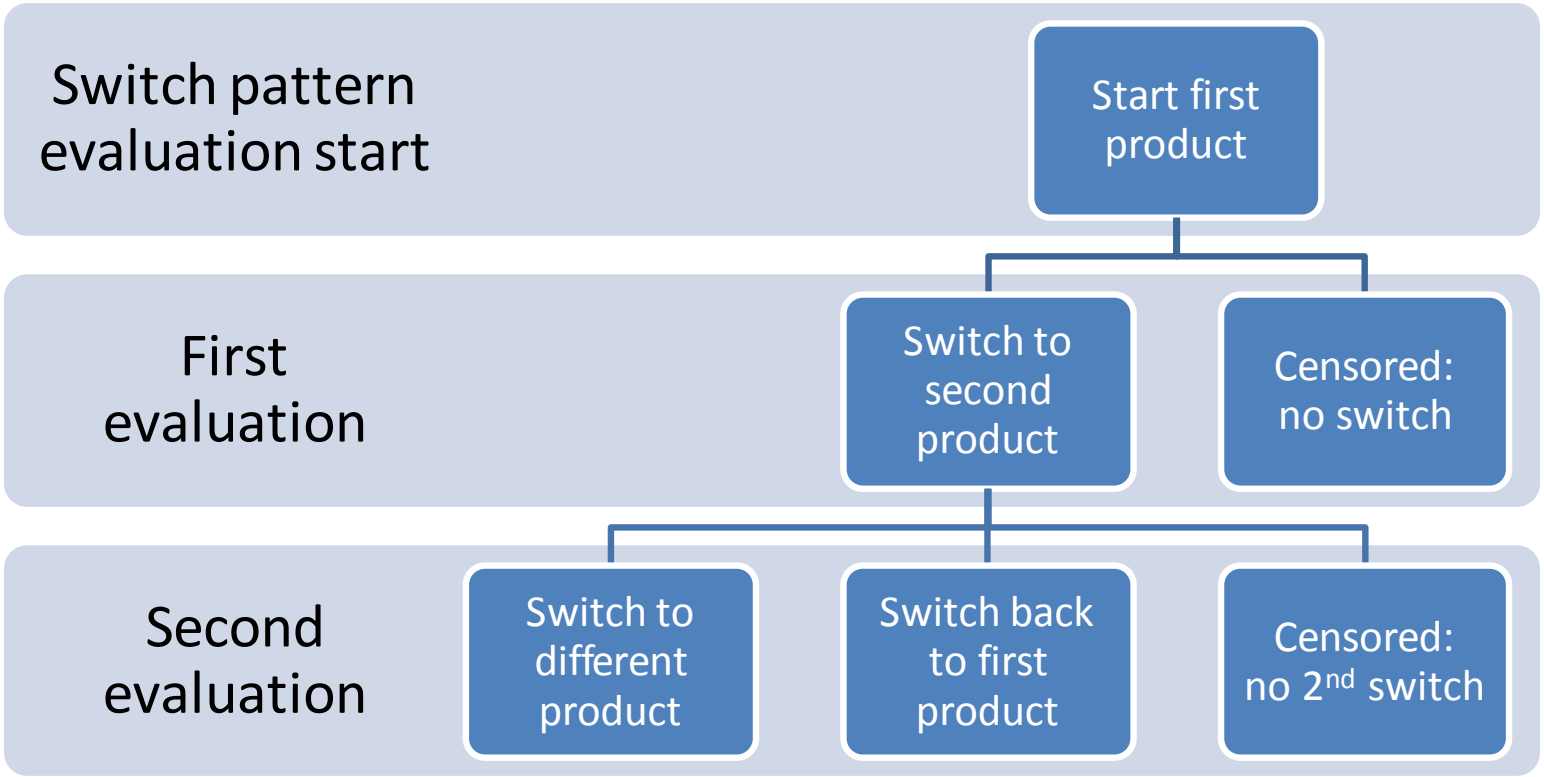
https://www.sentinelinitiative.org/

# Tool Development: Groups

- Captures utilization and switching patterns for user-specified groups
- Unit of analysis: user-specified groups
  - Defined by product national drug codes (NDCs) or procedure codes
  - Used to create treatment episodes, identify switching patterns, report utilization metrics
- For this analysis, groups were defined by manufacturer

Brand | Generic A | Generic B | Generic C

# Tool Development: Switching



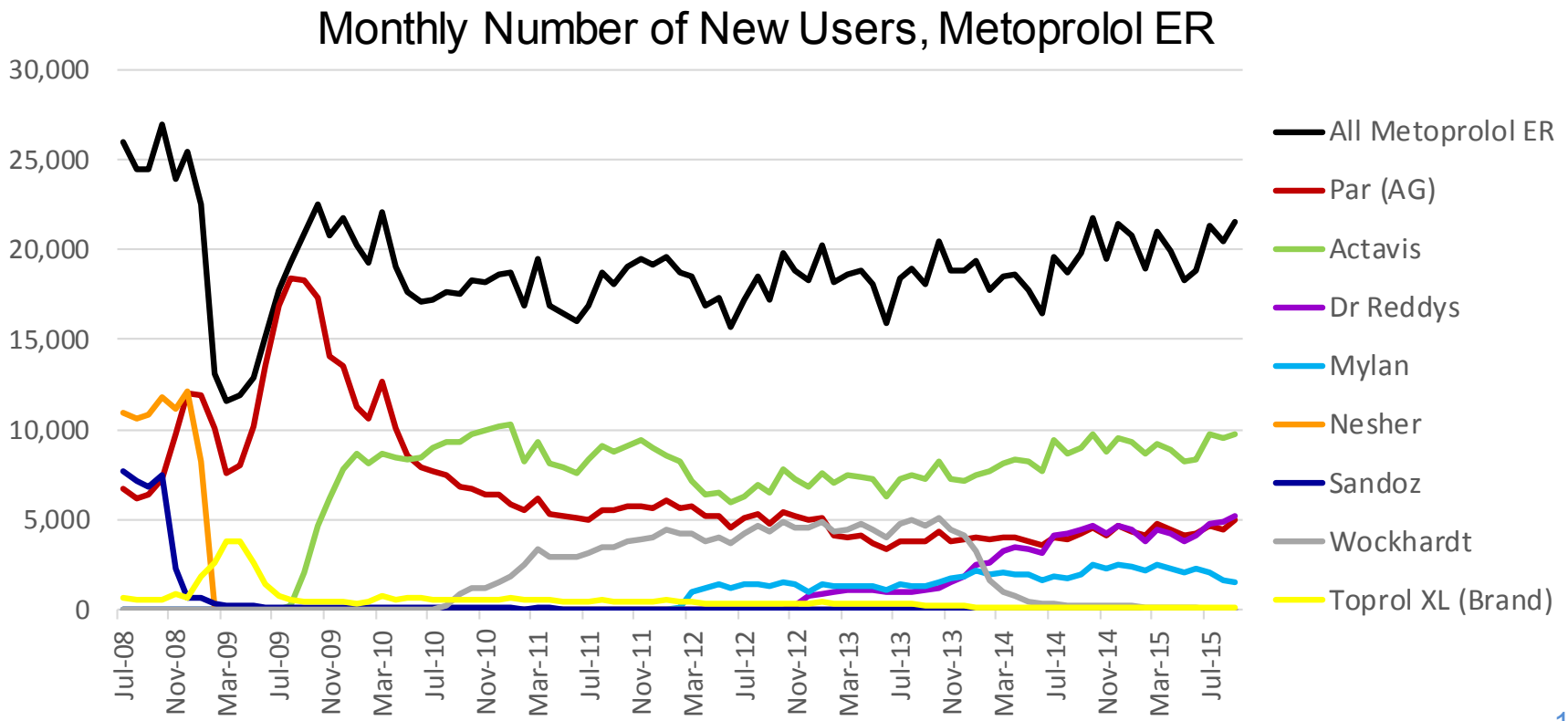
# Tool Development: Metrics

- Utilization metrics
  - Utilization over time
  - Summary statistics: product uptake, episode duration
- Switching metrics
  - Summary statistics
    - Time to 1st switch and 2nd switch
    - Switch pattern episode duration
  - Frequency distributions
    - People who switch, by months to 1st switch and to 2nd switch
  - Kaplan-Meier curves
    - Time to 1st switch and 2nd switch

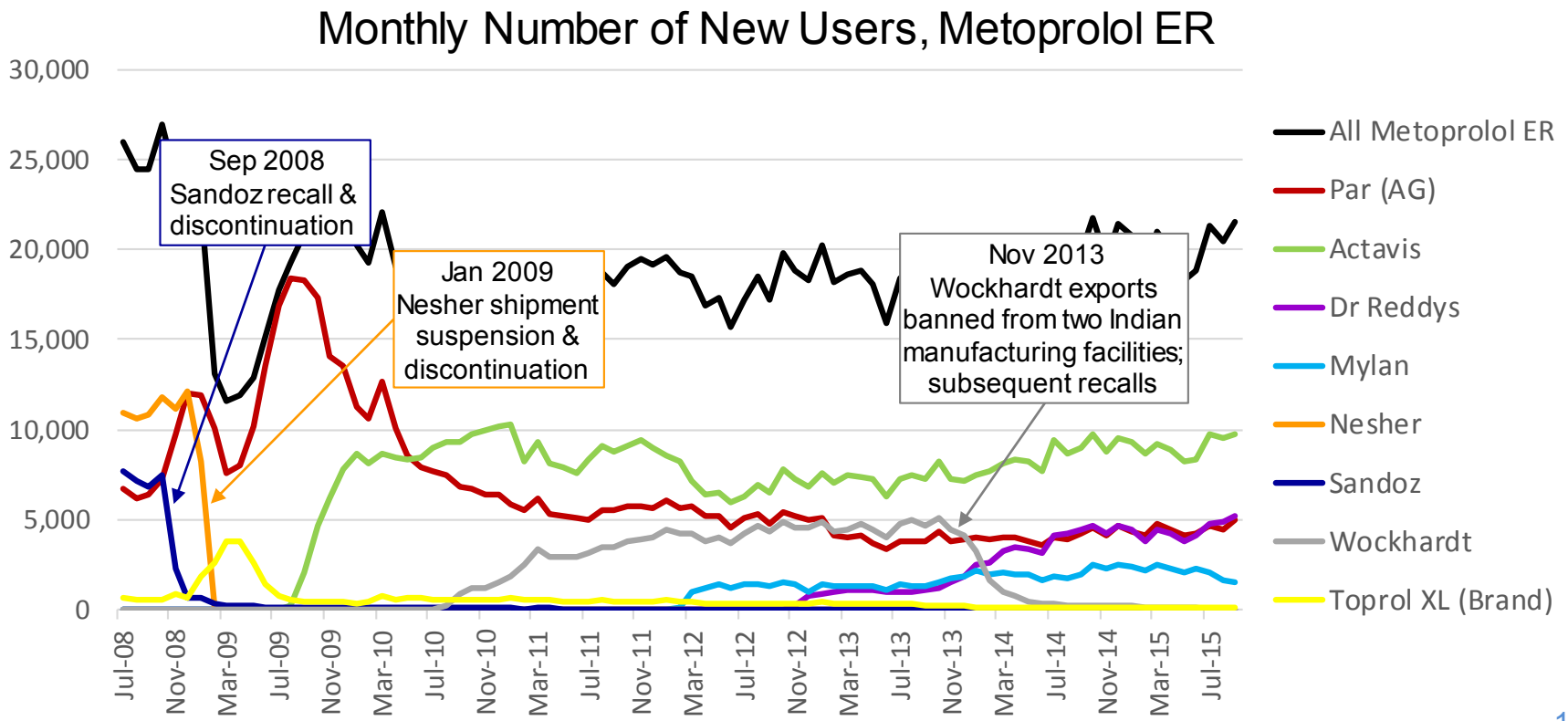
# Use Cases

1. Metoprolol extended release (ER)
   - Beta blocker indicated for the treatment of hypertension, angina pectoris, and heart failure
   - First generic was approved July 31, 2006
   - From 2008-2014, several manufacturers recalled some generic products due to failures meeting quality standards[10-13]
2. Lamotrigine ER
   - Anticonvulsant agent indicated for treatment of certain types of seizures in patients aged 13 years and older
   - First generic was approved December 26, 2012
   - Equivalence of generic antiepileptic drugs is an area of debate among healthcare providers[14,15]

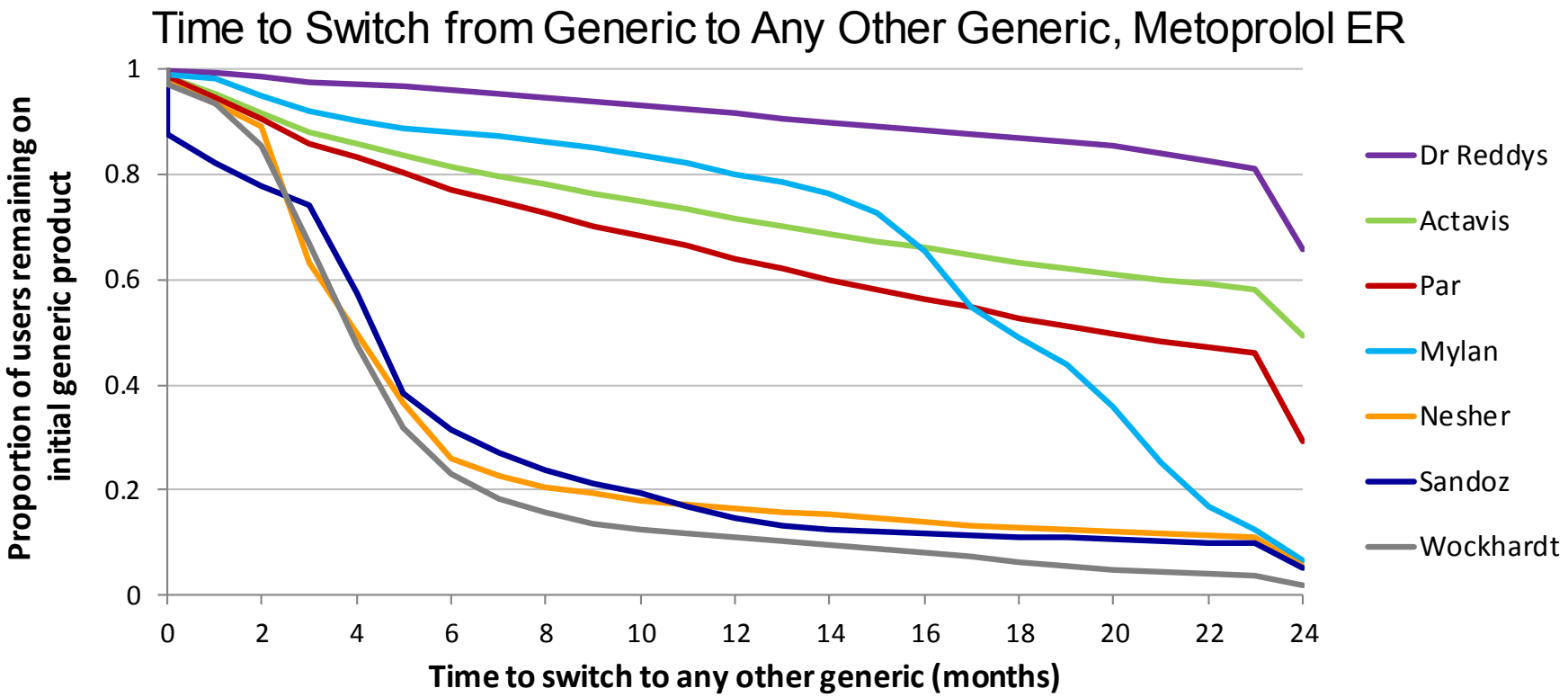
# Results: Metoprolol ER



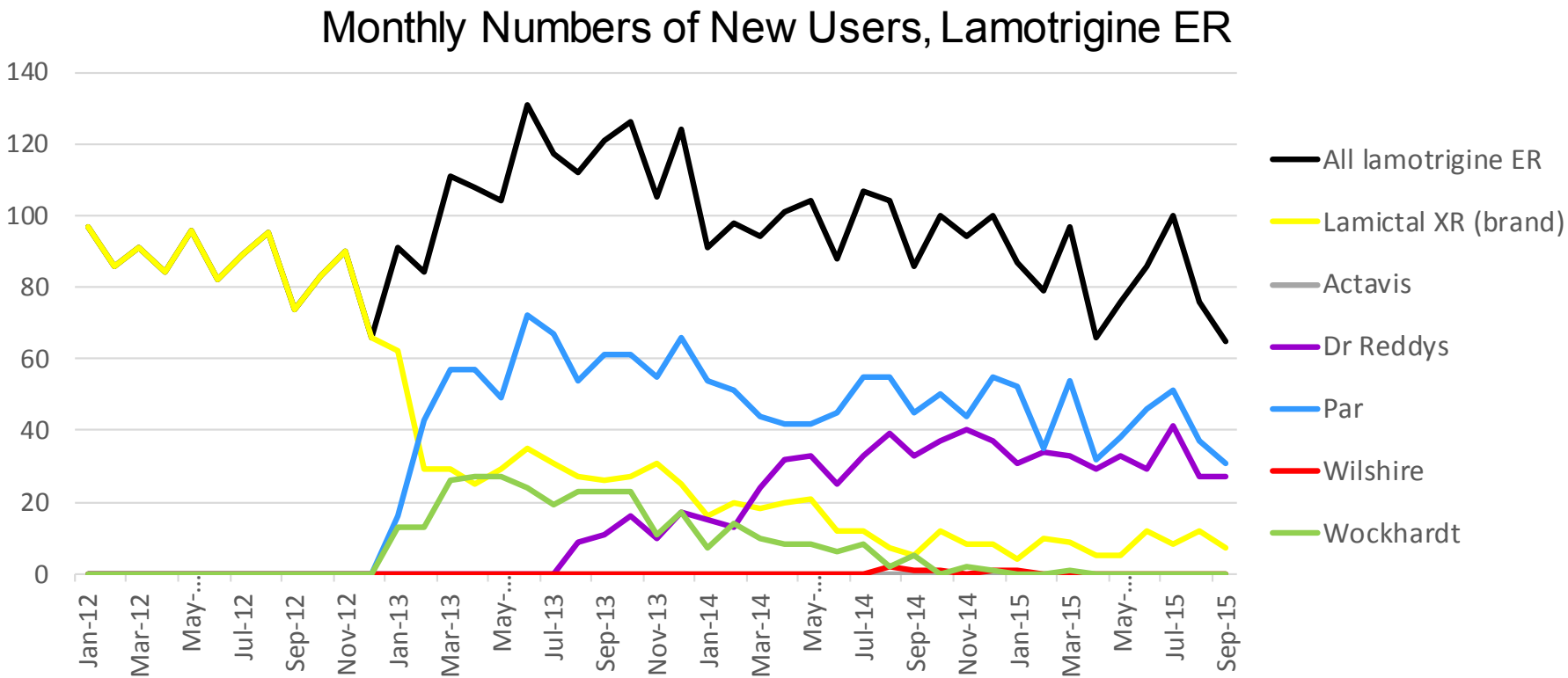
# Results: Metoprolol ER



# Results: Metoprolol ER



# Results: Lamotrigine ER



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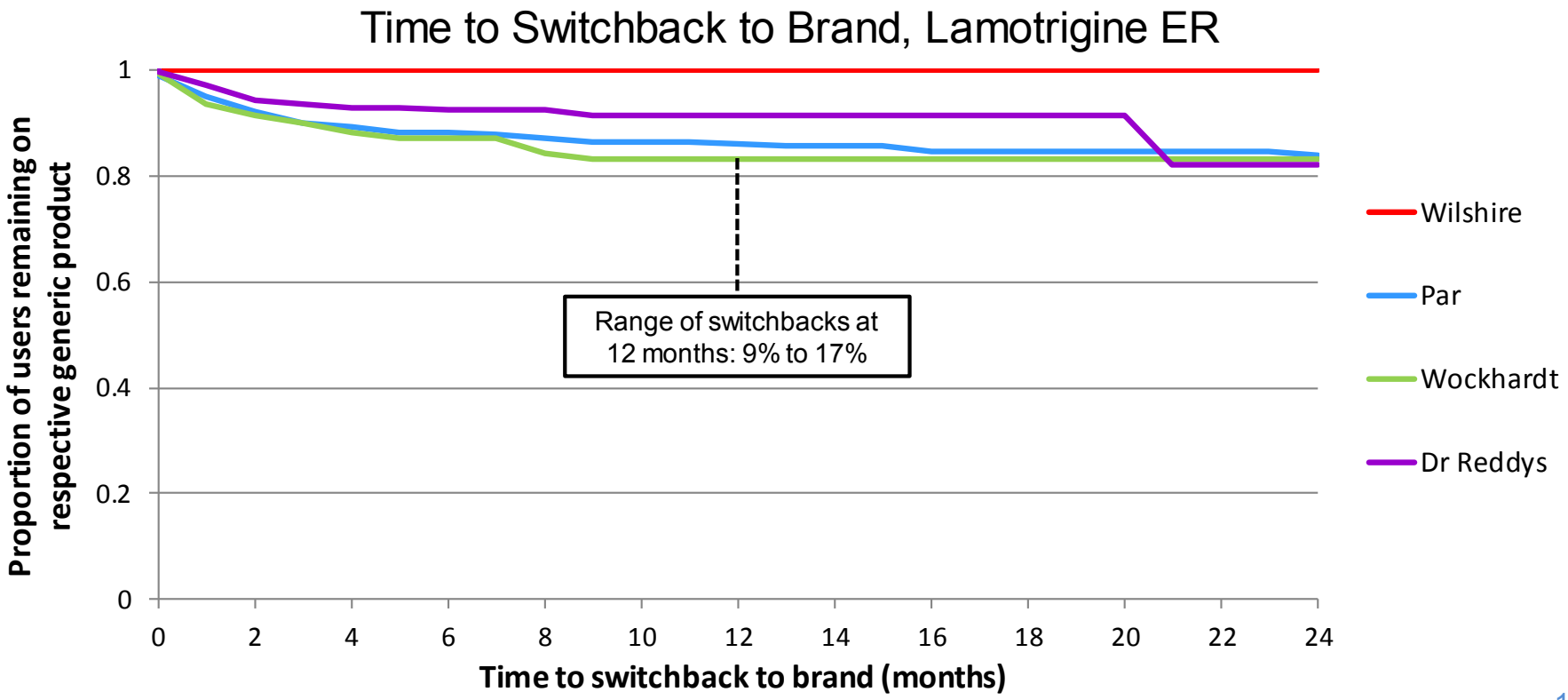

# Use Cases: Summary

- Metoprolol ER
  - Substantial changes in utilization following several manufacturer-specific production and availability issues
  - High rates of switching from generic products that were recalled and later discontinued
- Lamotrigine ER
  - Overall increase in use upon generic introduction
  - High rates of switchback from generic to brand: 9%-17% at 12 months
    - Consistent with previous studies, which found switchback rates of 13% – 28% for lamotrigine IR vs. 2% – 9% for antihyperlipidemics and antidepressants[5,6]

# Conclusions

- Successfully developed a reusable, parameterized, descriptive analysis tool to characterize manufacturer-level drug utilization and switching patterns within FDA's Sentinel System
- Tool confirmed expected utilization and switching patterns in 2 case studies
- Characterizing and evaluating switching or switchback patterns is potentially important in exploratory analyses of generic drugs and biosimilars in the postmarket setting
- Potential future enhancements:
  - Link this tool to existing tools for descriptive baseline cohort information
  - Evaluation of clinical outcomes associated with use of, or switching among, products from different manufacturers

# Acknowledgements


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

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