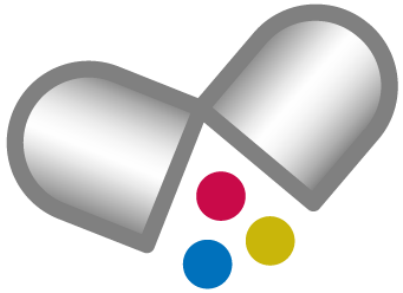

Measuring Key Deprescribing Variables from Electronic Health Data

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October 6, 2022

Disclosures

- The USDeN is funded by the National Institute on Aging, grant R24 AG064025
- Dr. Dublin has received research funding from GSK
- Dr. Hennessy has received funding through his employer from NIH, CDC, FDA, Pfizer, and Johnson and Johnson
  - Has consulted for Novo Nordisk, Arbor Pharmaceuticals, the Medullary Thyroid Cancer Consortium (Novo Nordisk, AstraZeneca, GlaxoSmithKline and Eli Lilly), Biogen, Intercept Pharmaceuticals, Provention Bio, bluebird bio, and Amylyx Pharmaceuticals
  - Is a special government employee of the FDA
- Dr. Maciejewski owns Amgen stock due to his spouse's employment and has received funding from NIH and the Department of Veterans Affairs
- Dr. Pham Nguyen receives support from Acadia Pharmaceuticals Inc.

Use of Electronic Health Data

- Clinical records (electronic medical records) and administrative/claims data
- Studies may use electronic data
  - To identify chronic medication users
  - To identify medication discontinuation
- It would be valuable to develop and evaluate methods for identifying medication discontinuation at scale using routinely collected health data

Why is Data Harmonization Needed?

- Different studies of deprescribing have used different criteria, which makes it difficult to compare and synthesize their results
- Health care systems are heterogeneous
- Different types of data: medication orders vs. medication fills
- Want to standardize measures as far as possible, to support rigor and validity

Data Harmonization Workgroup

- An activity of the US Deprescribing Research Network
- Collaboration of researchers at 5 healthcare systems
  - Integrated healthcare systems that provide both healthcare and insurance coverage
  - Academic health systems
  - US government system (Veterans Administration)
- Goal: To develop and demonstrate approaches to measure important variables for deprescribing studies across sites

Collaborators

- University of Pennsylvania: Sean Hennessy, Allison Willis, Danielle Mowery, Phuong Pham Nguyen, Sunil Thomas
- Kaiser Permanente Colorado: Elizabeth Bayliss, Lisa Pieper, Kathleen Albers
- Kaiser Permanente Washington: Sascha Dublin, Linda Kiel, Ladia Albertson-Junkans
- Duke University and Durham Veterans Administration: Matt Maciejewski, Susan Hastings, Juliessa Pavon, Amy Clark, Lindsay Zepel

Approach

- Key concepts we operationalized:
  - Chronic use of a medication
    - Benzodiazepines (BZD) and other sedative-hypnotics
  - Medication discontinuation
- Loosely based on an RCT, D-PRESCRIBE, that sought to help people stop these medications (Martin et al., JAMA 2018, PMID 30422193)
- Outpatient setting
- Study years: 2017-2019

Definition of Chronic Use

- From the source paper (Martin et al.):
  - Used data from pharmacies
  - Chronic use = one dispensing a month for 3 consecutive months
- Workgroup definition – claims data (dispensings)
  - ≥ 3 dispensings and total of ≥ 45 days supply within 100 days
  - Index date = date of the dispensing that results in meeting both of these criteria

Adapting Definition for Orders

- Challenges
  - A prescription may be ordered with a set number of refills allowed
  - New orders may not be needed for some time, as long as 1 yr
  - No information on days supply
  - Orders have an end date but this may be changed retroactively after the order was issued
- Workgroup definition adapted for orders data:
  - ≥ 3 prescriptions within 100 days, counting initial order and any allowed refills
    - E.g. 1 order with 2 refills included would count as 3
  - Index date = date of order (or refill) that results in meeting criteria

Results: Chronic Use

Criterion	Site A	Site B	Site C (orders)	Site D	Site E
Age 65+, adequate enrollment	51,417	90,186	129,678	99,335	22,301
Chronic BZD or Z-drug use in 2018	806 (1.6%)	2310 (2.6%)	1886 (1.5%)	2432 (2.4%)	505 (2.3%)

How do results differ when chronic use is determined from orders vs. fills?

Hypothesis: use of orders may overestimate chronic use, since people may receive a prescription but not fill it, or may not use refills that were allowed

Approach

- Analyses carried out within Kaiser Permanente Washington
  - Orders and fills are available for the same population
- Identified order-based and fill-based definitions to the same individuals in the same time period
- Examined the overlap

Comparing Chronic Use based on Orders vs. Fills

	Defined from Medication Fills		
Defined from Orders	No chronic use	Chronic use	Total
No chronic use	0	78	78
Chronic use	471	603	1074
Total	471	681	N=1152

- Limited to people who qualified under one or both definitions
- Of chronic use defined from orders, ~55% is also confirmed via fills data.
- Most chronic use defined from fills also meets criteria based on orders (~90%) .

Stratified by Number of Orders

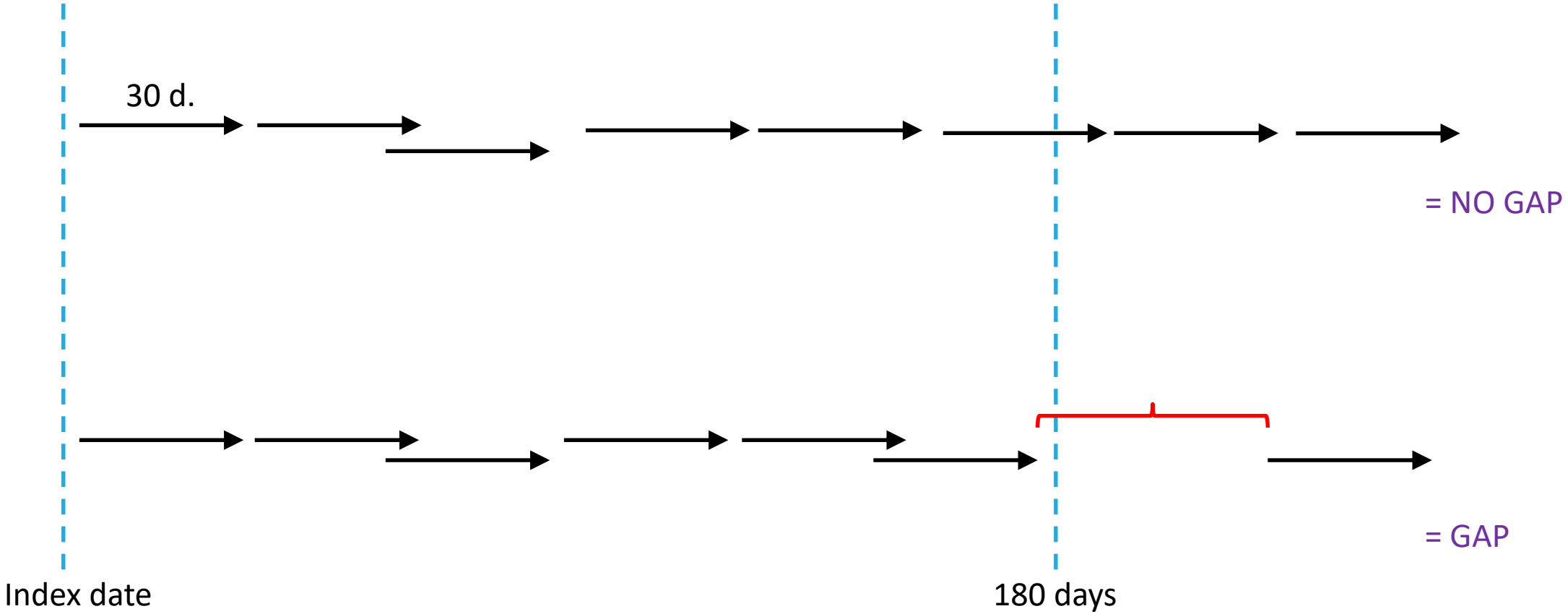
Number of Orders Per Patient	Total Meeting Orders Criteria for Chronic Use	Also Meet Fills Criteria for Chronic Use	Proportion Meeting Fills Criteria for Chronic Use
1	458	169	37%
2	80	40	50%
3	536	377	70%
4	19	10	53%

Definition of Medication Discontinuation

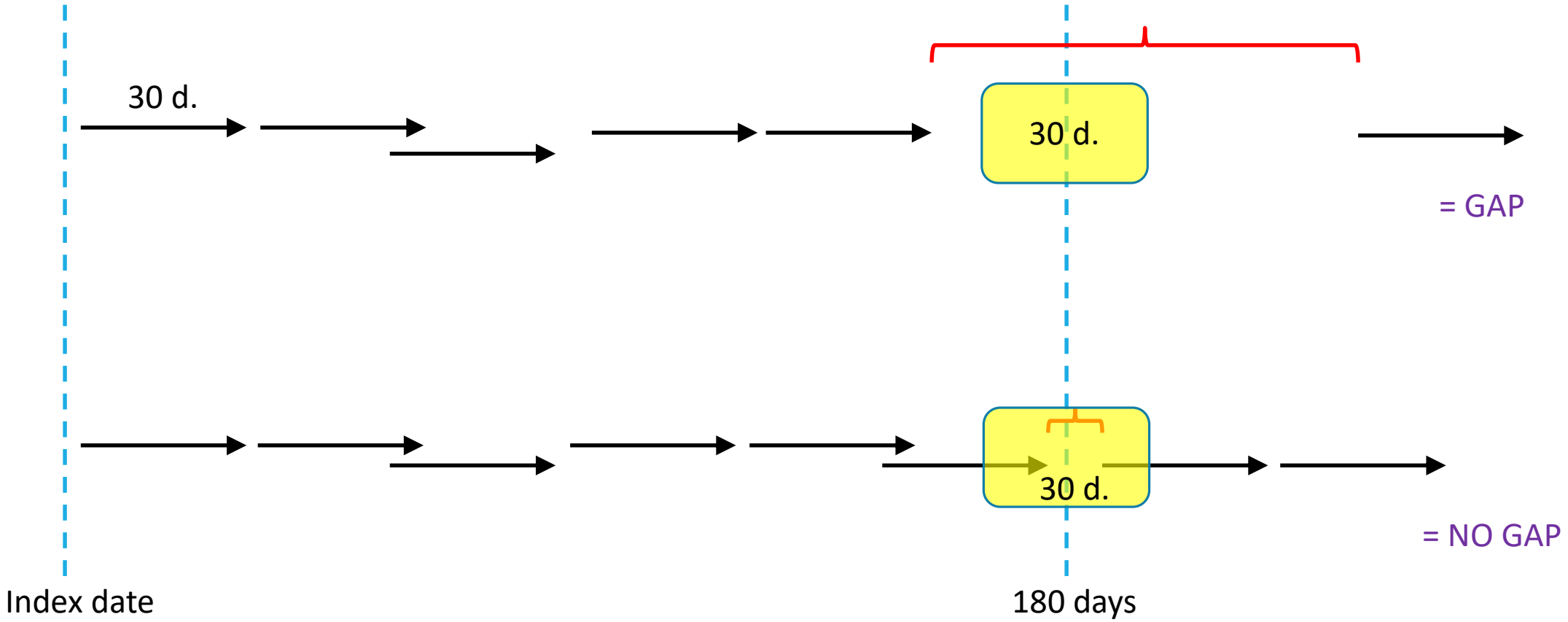
- Two approaches
- Gaps: Did a person have a gap in use of XX days over a 1 year follow up period?
  - Varying length of gap required (30, 60, 90, 180 days)
  - Varying whether we accounted for stockpiling, i.e., “early” fills overlapping with a prior fill*
- Continued use at a fixed point:
  - At a given time point during follow up, did a person appear to have any of the medication on hand?
  - Varied the time point (180, 270, 365 days)
  - Variation: applying a 30-day “halo” around the fixed point and requiring no dispensings or orders within that 30 day “halo”

*Only applies to fills data.

Illustration of Fixed-Point Definition

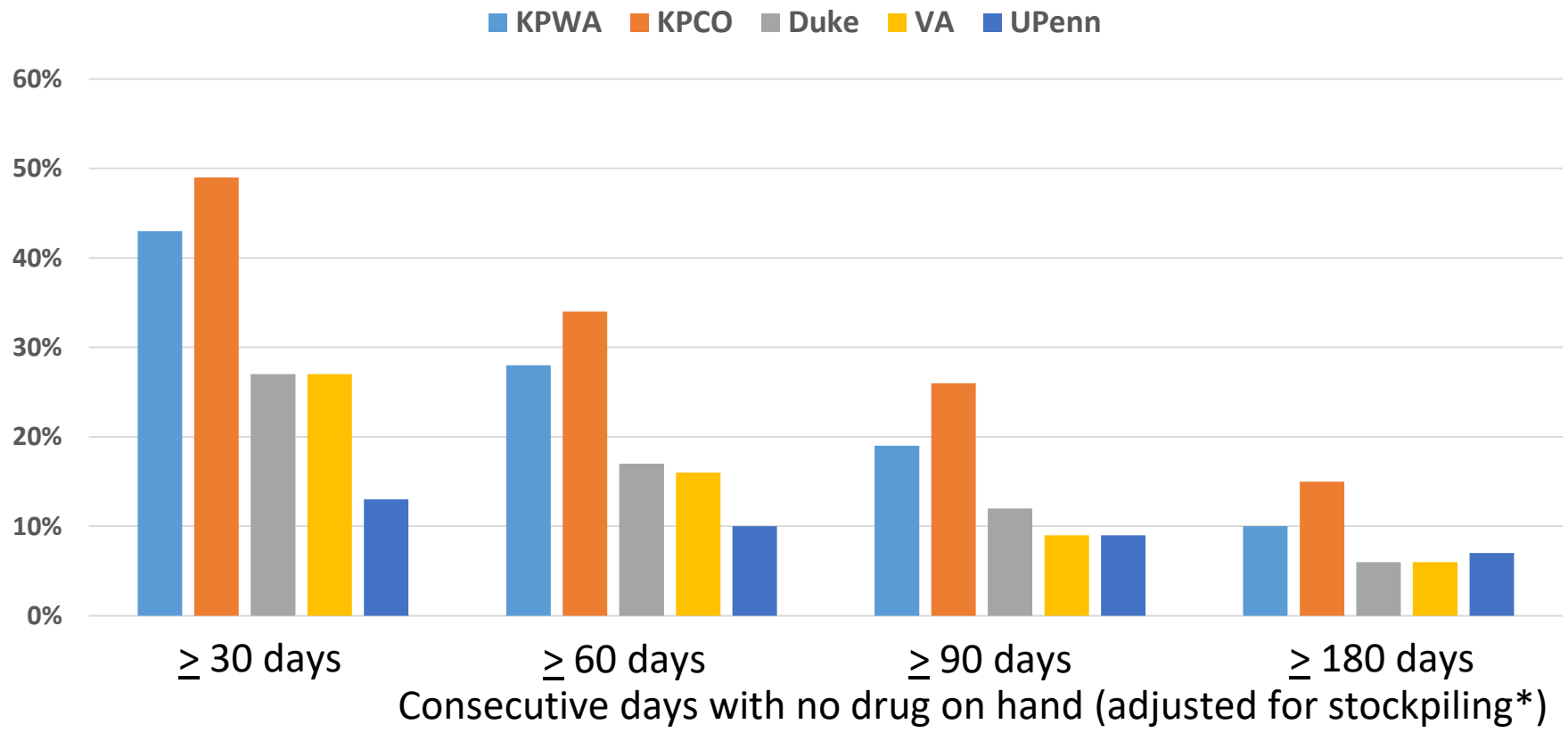


Fixed-Point Definition, with Halo



Comparison of Gap-Based Definitions, Varying the Length of the Gap

% of people who discontinued decreases when moving from shorter gap (≥30 days) to longer gap (≥180 days)

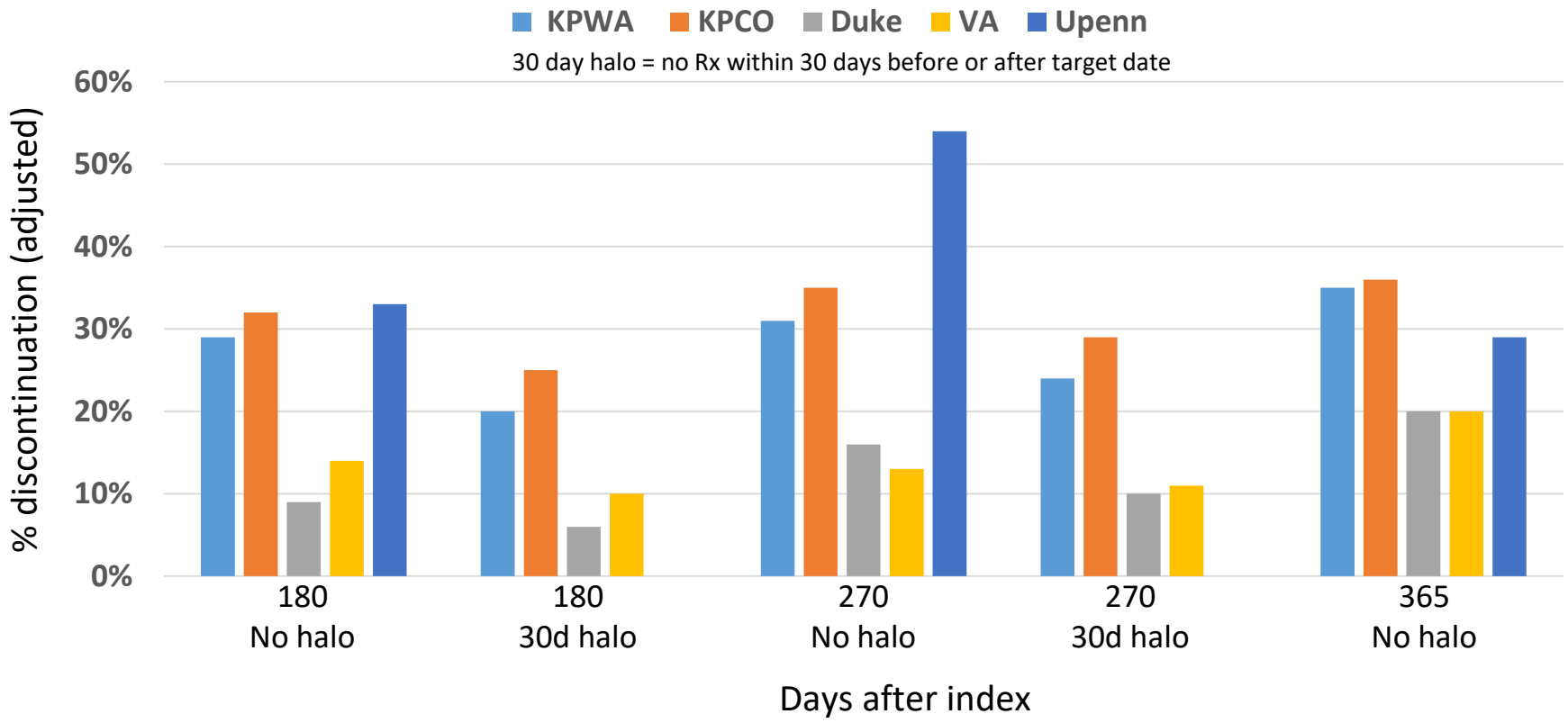


*Note: UPenn is unadjusted due to use of orders data. All other sites are adjusted/ fill data

Comparison of Fixed Point Definitions with varying times after index (w/ & w/o halo)

% of people who discontinued increases with increasing time since index date

- 30-day “halo” around end date decreases % meeting definition

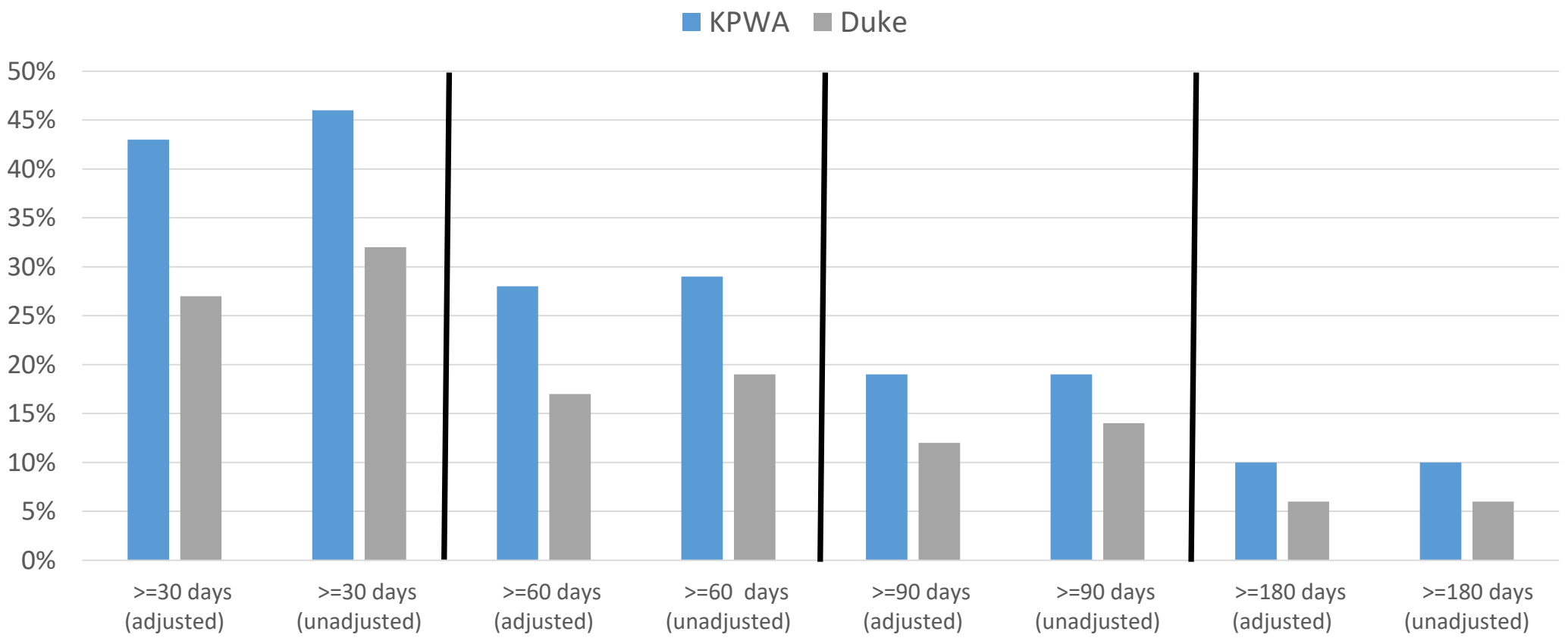


*Note: UPenn is unadjusted due to use of orders data. All other sites are adjusted/ fill data

Is it important to account for stockpiling?

Gap-Based Definitions: Impact of Adjusting for Stockpiling

Discontinuation rates consistently lower with adjustment for stockpiling



*Note: other sites excluded to simplify

Recommendations

- When looking for a gap in use at any point in follow up, a 30-day gap is probably not long enough to feel confident it represents true discontinuation
- General consensus was that a gap ≥ 90 days was preferred
  - Likely vary by drug class
- If defining discontinuation at a fixed point in time, would recommend the “halo” approach as many people had a fill or order close to the “fixed point” of interest
- Accounting for stockpiling mattered, and it was more influential when the length of the gap was short

Challenges and Learnings

- Healthcare systems have different systems for classifying medications
  - Commercial lists of drug codes/classes are proprietary and expensive
- Working with orders is difficult; how to infer “days supply”?
- Dispensing data are much cleaner and can more easily identify discontinuation
- Data on fills are preferable to order data, when possible, given the challenges in characterizing a stop from orders data
- Difficult to distinguish between imperfect adherence and discontinuation, especially for shorter gaps
- Cannot distinguish supported and clinically appropriate discontinuation vs. unsupervised non-persistence/abandonment

Next Steps

- Drafting a manuscript based on findings
- Writing a practical “how-to” guide containing more detail about the actual programming approach
  - By lead programmer for the workgroup
- US Deprescribing Research Network: deprescribingresearch.org

Areas for Future Research

- Validating algorithms for discontinuation against other sources such as medical records or patient interviews
- Identifying dose reduction
- Develop definitions for other settings such as inpatient setting or skilled nursing facilities
  - Very different data and time scale (daily data)

DeprescribingResearch.org