Thinking Globally While Acting Locally: Developing Time-on-treatment Data in International Settings

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August 26, 2019

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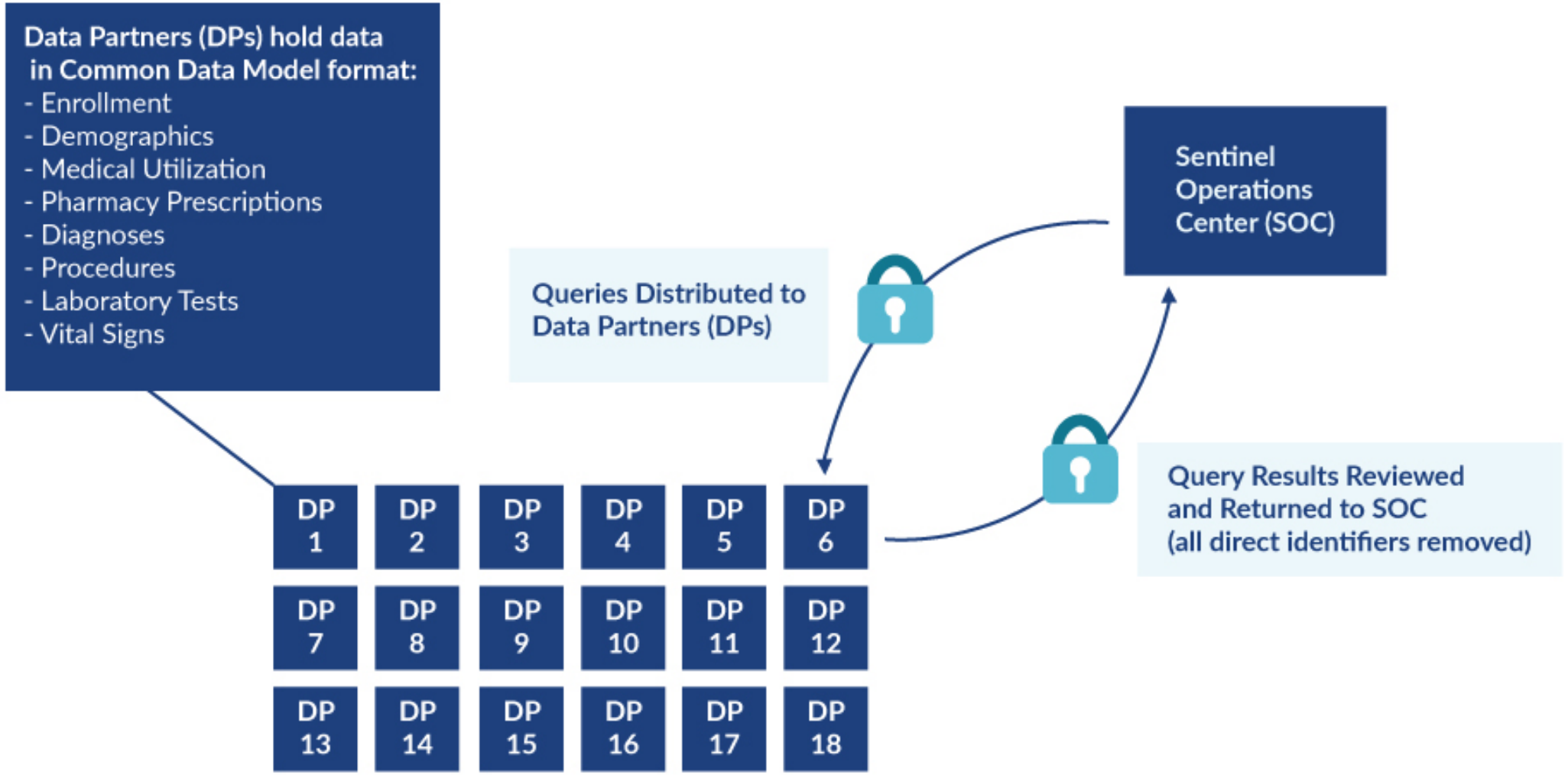
Disclosures

- I have no conflicts to disclose.
- I receive funding from the U.S. Food and Drug Administration under HHSF223201400030I.

Acknowledgements: We would like to acknowledge all the Data Partners that contributed data.

Sentinel is a Distributed Data Network



https://www.sentinelinitiative.org/sentinel/sentinels-distributed-database

Available Data Elements

Administrative Data

Enrollment	Demographic	Dispensing	Encounter	Diagnosis	Procedure
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth Date	Dispensing Date	Service Date(s)	Service Date(s)	Service Date(s)
Drug Coverage	Sex	National Drug Code (NDC)	Encounter ID	Encounter ID	Encounter ID
Medical Coverage	Zip Code	Days Supply	Encounter Type and Provider	Encounter Type and Provider	Encounter Type and Provider
Medical Record Availability	Etc.	Amount Dispensed	Facility	Diagnosis Code & Type	Procedure Code & Type
			Etc.	Principal Discharge Diagnosis	Etc.

Clinical Data

Lab Result	Vital Signs
Patient ID	Patient ID
Result & Specimen Collection Dates	Measurement Date & Time
Test Type, Immediacy & Location	Height & Weight
Logical Observation Identifiers Names and Codes (LOINC®)	Diastolic & Systolic BP
Etc.	Tobacco Use & Type
	Etc.

Registry Data

Death	Cause of Death	State Vaccine
Patient ID	Patient ID	Patient ID
Death Date	Cause of Death	Vaccination Date
Source	Source	Admission Date
Confidence	Confidence	Vaccine Code & Type
Etc.	Etc.	Provider
		Etc.

Inpatient Data

Inpatient Pharmacy	Inpatient Transfusion
Patient ID	Patient ID
Administration Date & Time	Administration Start & End Date & Time
Encounter ID	Encounter ID
National Drug Code (NDC)	Transfusion Administration ID
Route	Transfusion Product Code
Dose	Blood Type
Etc.	Etc.

Mother-Infant Linkage Data

Mother-Infant Linkage
Mother ID
Mother Birth Date
Encounter ID & Type
Admission & Discharge Date
Child ID
Child Birth Date
Mother-Infant Match Method
Etc.

https://www.sentinelinitiative.org/sentinel/data/distributed-database-common-data-model

Single Patient Example Data in Model

DEMOGRAPHIC

PATID	BIRTH_DATE	SEX	HISPANIC	RACE	zip
PatID1	2/2/1964	F	N	5	32818

DISPENSING

PATID	RXDATE	NDC	RXSUP	RXAMT
PatID1	10/14/2005	00006074031	30	30
PatID1	10/14/2005	00185094098	30	30
PatID1	10/17/2005	00378015210	30	45
PatID1	10/17/2005	54092039101	30	30
PatID1	10/21/2005	00173073001	30	30
PatID1	10/21/2005	49884074311	30	30
PatID1	10/21/2005	58177026408	30	60
PatID1	10/22/2005	00093720656	30	30
PatID1	10/23/2005	00310027510	30	15

ENROLLMENT

PATID	ENR_START	ENR_END	MEDCOV	DRUGCOV
PatID1	7/1/2004	12/31/2004	Y	N
PatID1	1/1/2005	12/31/2005	Y	Y

DEATH

PATID	DEATHDT	DTIMPUTE	SOURCE	CONFIDENCE
PatID1	12/27/2005	N	S	E

ENCOUNTER

PATID	ENCOUNTERID	ADATE	DDATE	ENCTYPE
PatID1	EncID1	10/18/2005	10/20/2005	IP

DIAGNOSIS

PATID	ENCOUNTERID	ADATE	PROVIDER	ENCTYPE	DX	DX_CODETYPE	PDX
PatID1	EncID1	10/18/2005	Provider1	IP	296.2	9	P
PatID1	EncID1	10/18/2005	Provider1	IP	300.02	9	S
PatID1	EncID1	10/18/2005	Provider1	IP	305.6	9	S
PatID1	EncID1	10/18/2005	Provider1	IP	311	9	P
PatID1	EncID1	10/18/2005	Provider1	IP	401.9	9	S
PatID1	EncID1	10/18/2005	Provider1	IP	493.9	9	S
PatID1	EncID1	10/18/2005	Provider1	IP	715.9	9	S

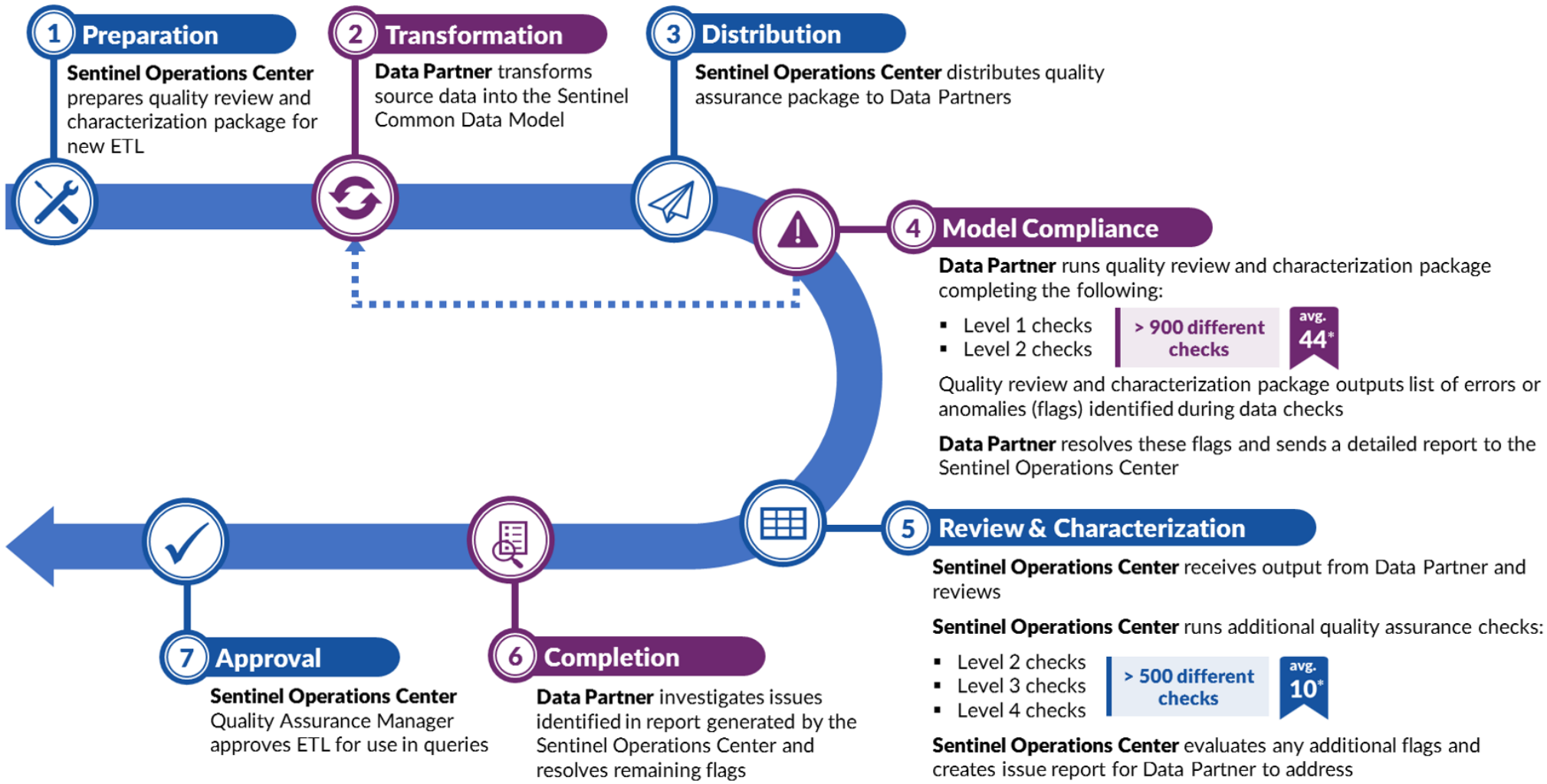
PROCEDURE

PATID	ENCOUNTERID	ADATE	PROVIDER	ENCTYPE	PX	PX_CODETYPE
PatID1	EncID1	10/18/2005	Provider1	IP	84443	C4
PatID1	EncID1	10/18/2005	Provider1	IP	99222	C4
PatID1	EncID1	10/18/2005	Provider1	IP	99238	C4
PatID1	EncID1	10/18/2005	Provider2	IP	27445	C4

CAUSE OF DEATH

PATID	COD	CODETYPE	CAUSETYPE	SOURCE	CONFIDENCE
PatID1	J18.0	10	U	S	E

Data Quality Review and Characterization Process



* On average, there are 44 flags identified by the program and 10 additional flags identified by the Sentinel Operations Center per ETL

https://www.sentinelinitiative.org/sentinel/data-quality-review-and-characterization

Sentinel Data Philosophy

- Includes claims, electronic health record (EHR), and registry data and flexible enough to accommodate new data domains (e.g., free text).
  - Typically, we do not include empty tables – we expand as needed when fit for purpose.
- Data are stored at most granular/raw level possible with minimal mapping.
  - Distinct data types should be kept separate (e.g., prescriptions, dispensings)
  - Construction of medical concepts (e.g., outcome algorithms) from these elemental data is a project-specific design choice.
  - Sentinel stores these algorithms in a library for future use.
- Appropriate use and interpretation of local data requires the Data Partners' local knowledge and data expertise.
  - Not all tables are populated by all Data Partners➔site-specificity is allowed.
- Designed to meet FDA needs for analytic flexibility, transparency, and control.

Piloting “North American” Distributed Data Networks

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Administrative Data						Registry Data
Enrollment	**Demographic**	**Dispensing**	**Encounter**	**Diagnosis**	**Procedure**	**Death**
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth Date	Dispensing Date	Service Date(s)	Service Date(s)	Service Date(s)	Death Date
Drug Coverage	Sex	Dispensing Code and Type	Encounter ID	Encounter ID	Encounter ID	Source
Medical Coverage	Zip Code	Days Supply	Encounter Type and Provider	Encounter Type and Provider	Encounter Type and Provider	Confidence
Medical Record Availability	Etc.	Amount Dispensed	Facility	Diagnosis Code & Type	Procedure Code & Type	Etc.
			Etc.	Principal Discharge Diagnosis	Etc.	

Comparative Advantages: Longer Follow-Up Time

https://www.sentinelinitiative.org/sentinel/data/distributed-database-common-data-model

CNODES Common Data Model Pilot Project

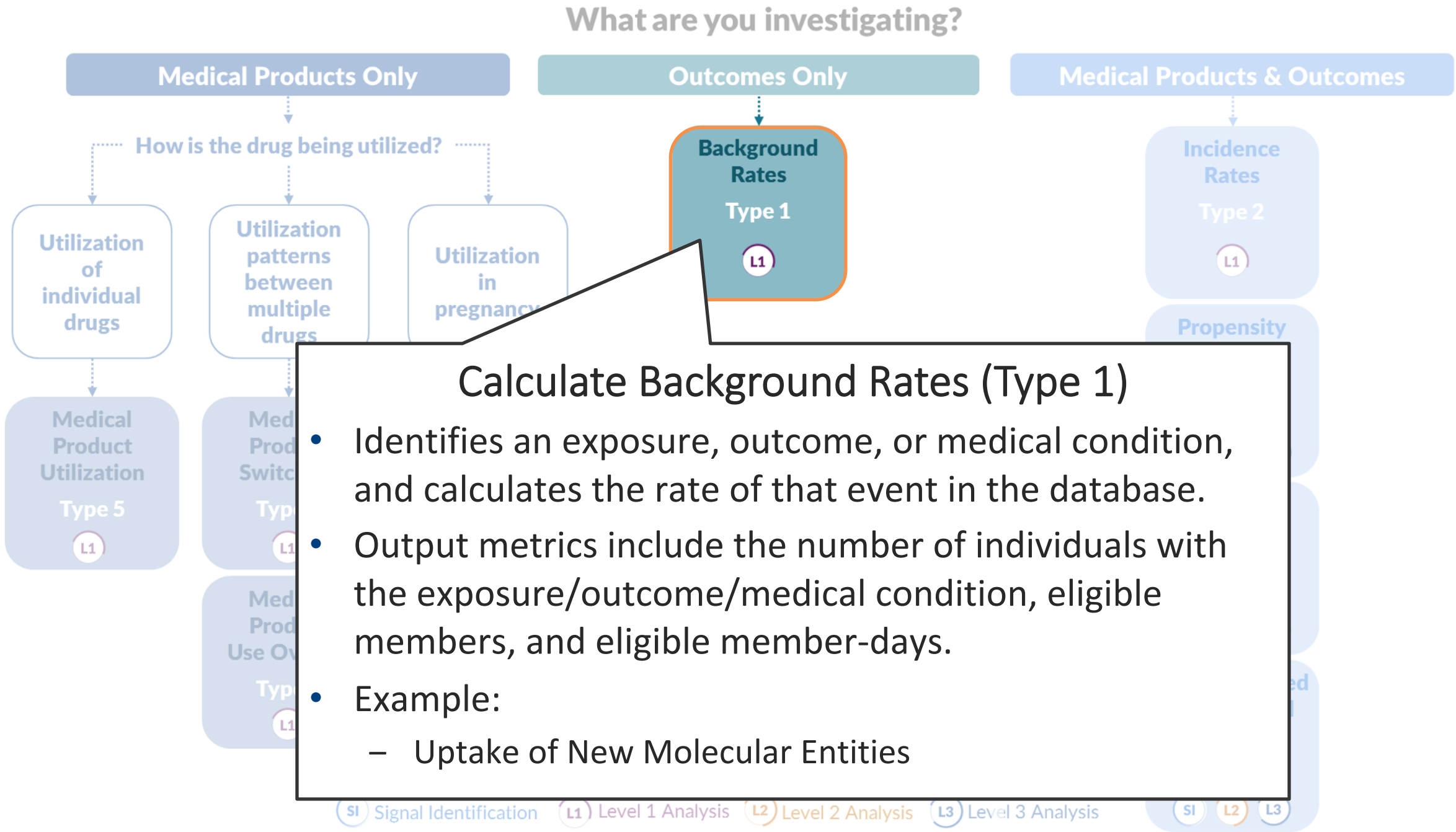
- Four Provinces (Saskatchewan, Manitoba, Ontario, Nova Scotia)
- Converted Administrative Data Tables and Death Table
  - Four quality assurance packages run at individual provinces; all passed
- Ready for querying using standard tools
  - One demonstration query looked at uptake of New Molecular Entities (NMEs) approved in 2015 in Canada
  - Equivalent queries were run in the Sentinel Distributed Database for other NME cohort years

https://www.ema.europa.eu/en/documents/presentation/presentation-session-3-cnodes-common-data-model-pilot-project-challenges-opportunities-robert-platt_en.pdf

Active Risk Identification and Analysis (ARIA)

- Template computer programs with standardized questions
- Parameterized at program execution
- Pre-tested and quality-checked
- Standard output

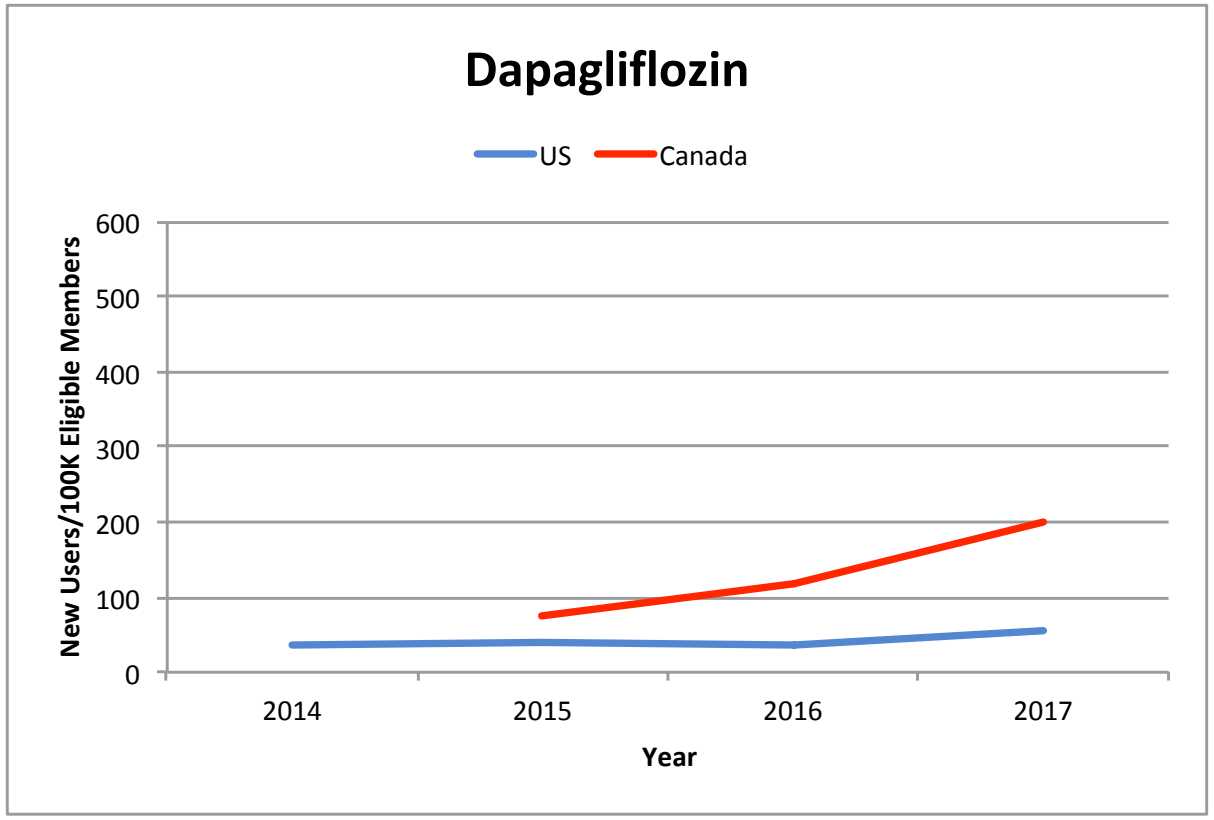
https://www.sentinelinitiative.org/active-risk-identification-and-analysis-aria

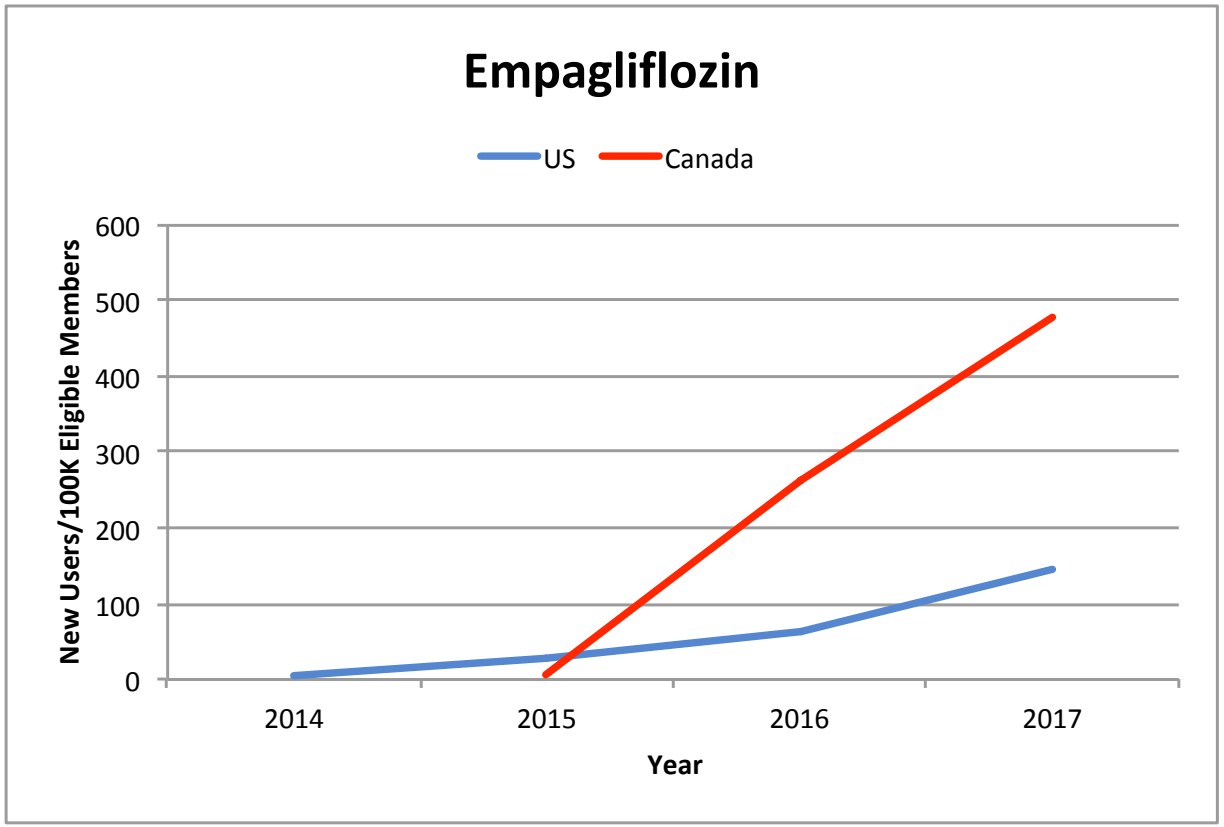


Calculate Background Rates (Type 1)

- Identifies an exposure, outcome, or medical condition, and calculates the rate of that event in the database.
- Output metrics include the number of individuals with the exposure/outcome/medical condition, eligible members, and eligible member-days.
- Example:
  - Uptake of New Molecular Entities

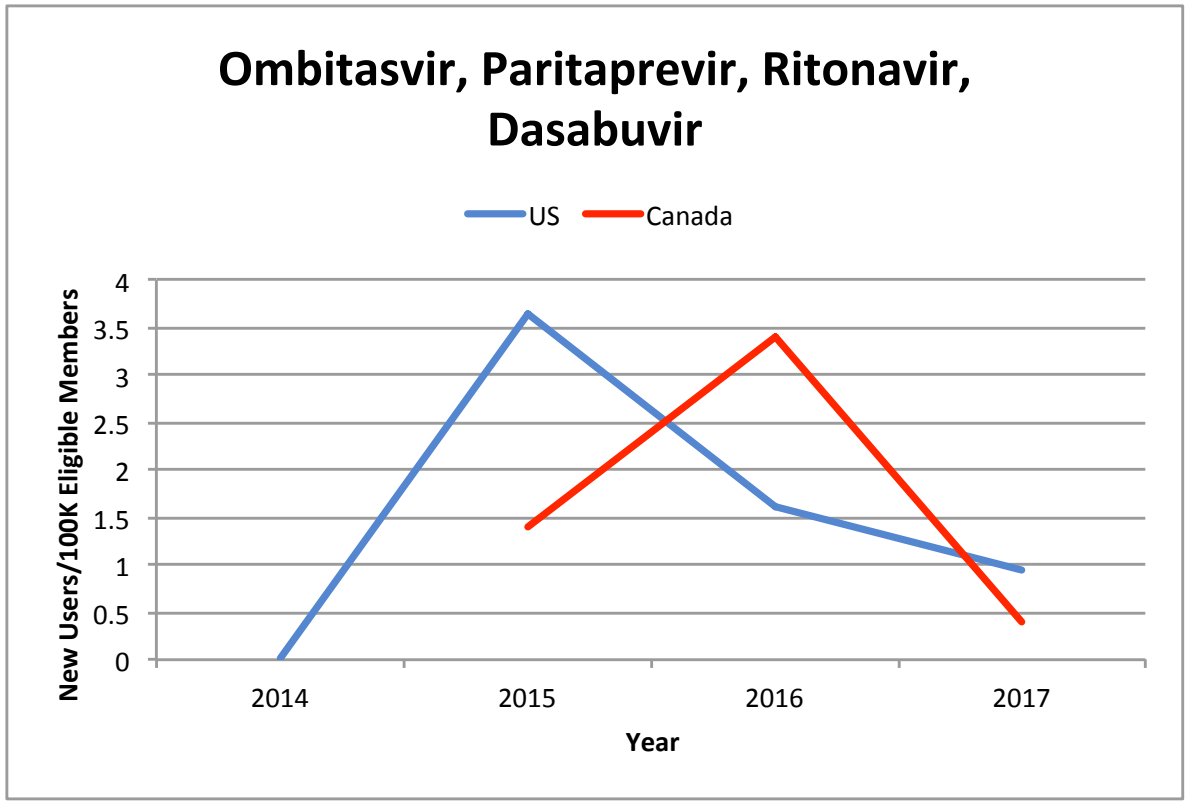
2015 New Molecular Entities – High Prevalence Medicines

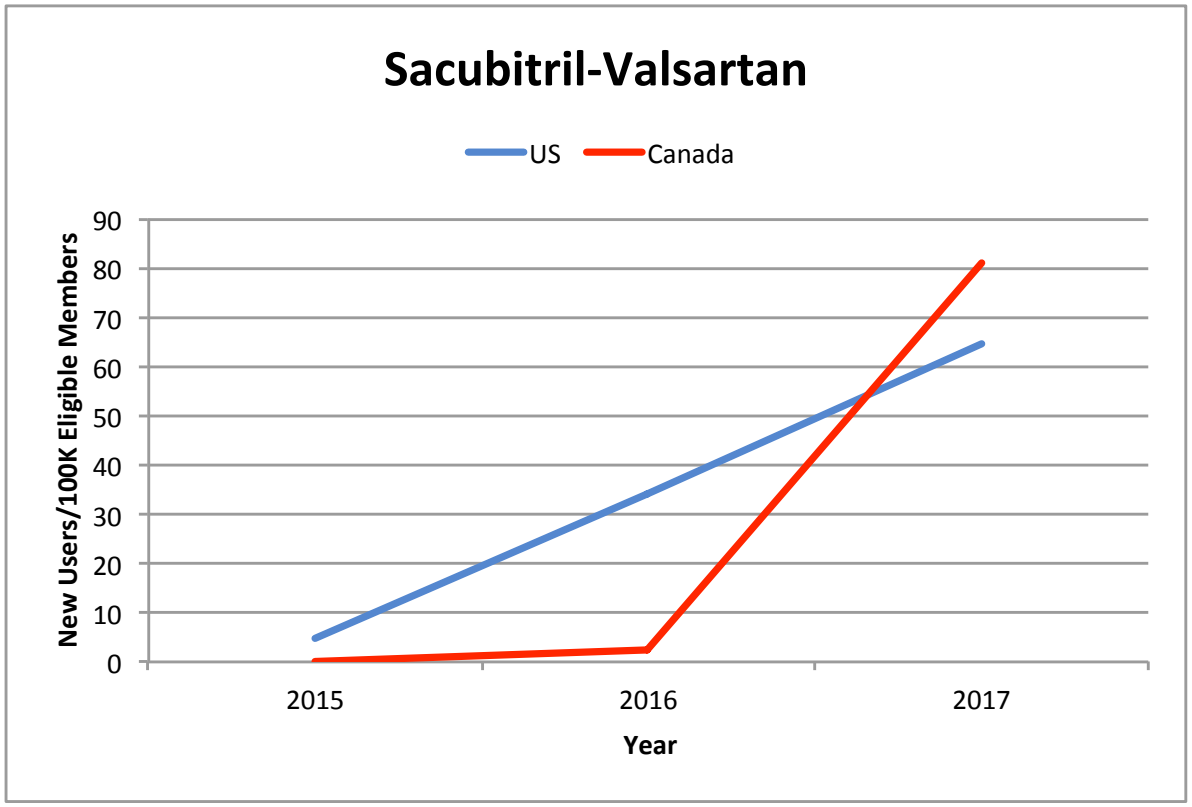




Observations: US v Canada

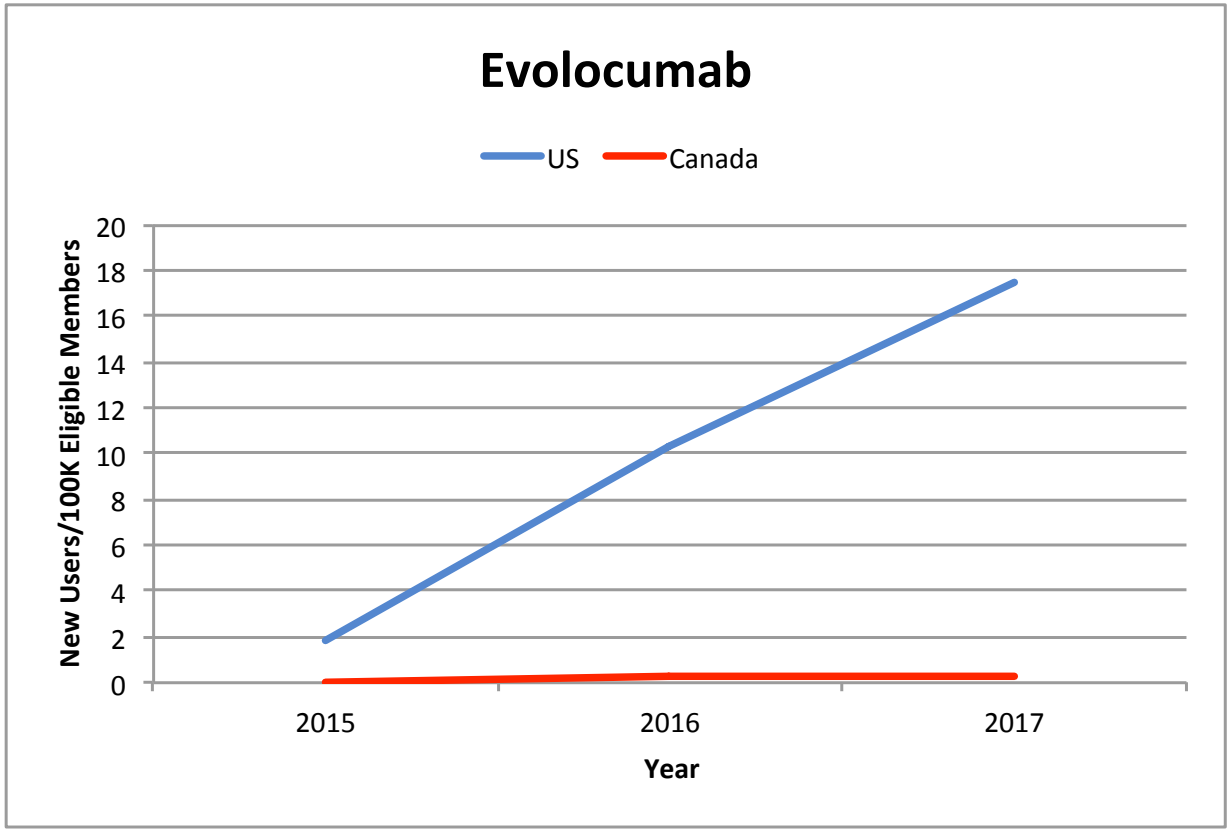
2015 New Molecular Entities – High Cost Medications

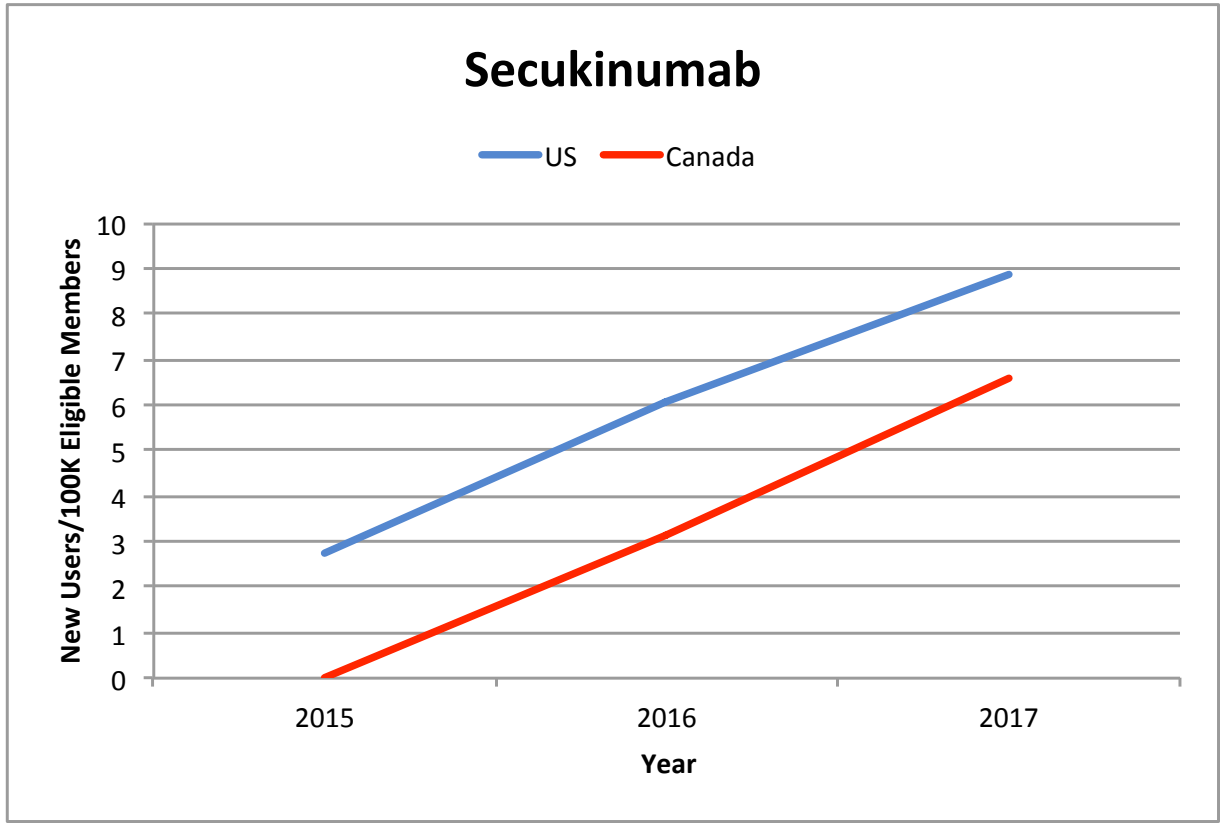




Observations: US v Canada

2015 New Molecular Entities – Injectables

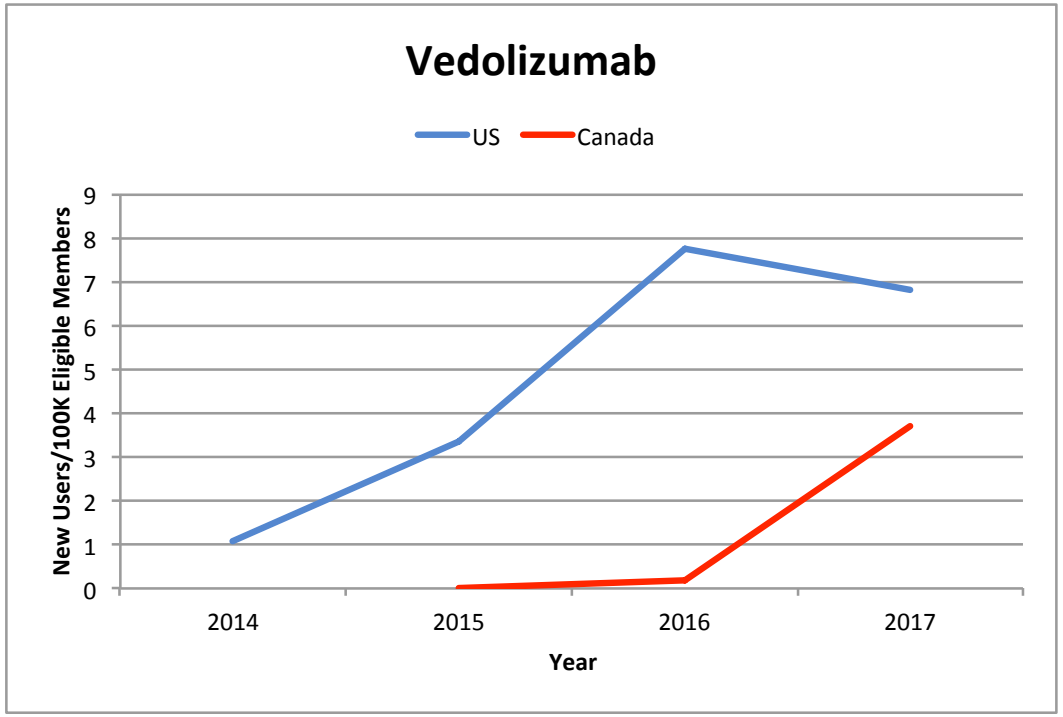




Observations: US v Canada

2015 New Molecular Entities – Administered Medicines

- Medicines Not Well Captured in Canadian Data
  - Checkpoint Inhibitors (e.g., pembrolizumab, nivolumab)
  - Selected Oncology Drugs (e.g., ramucirumab)



Observations: US v Canada

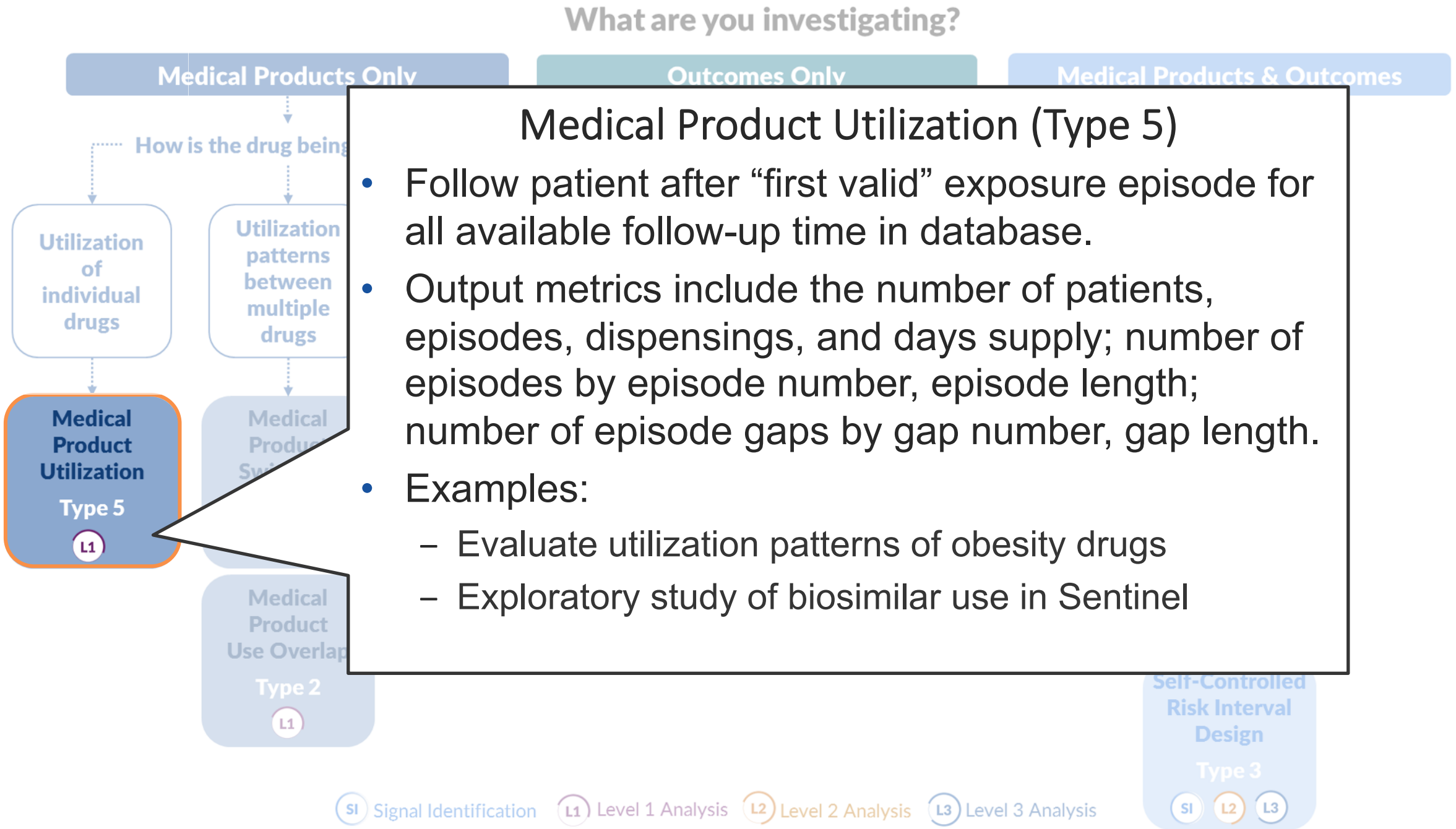
Simple Proof-of-Concept Prescribing Table for CPRD

UK data driving real-world evidence

Administrative Data					
Enrollment	**Demographic**	**Prescribing**	**Encounter**	**Diagnosis**	**Procedure**
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth Date	Prescription Date	Service Date(s)	Service Date(s)	Service Date(s)
Drug Coverage	Sex	Prescribing Code & Type	Encounter ID	Encounter ID	Encounter ID
Medical Coverage	Zip Code	Days Supply	Encounter Type and Provider	Encounter Type and Provider	Encounter Type and Provider
Medical Record Availability	Etc.	Amount Prescribed	Facility	Diagnosis Code & Type	Procedure Code & Type
			Etc.	Principal Discharge Diagnosis	Etc.

Comparative Advantages: Longer Follow-up Time, General Practitioner Intent

https://www.sentinelinitiative.org/sentinel/data/distributed-database-common-data-model



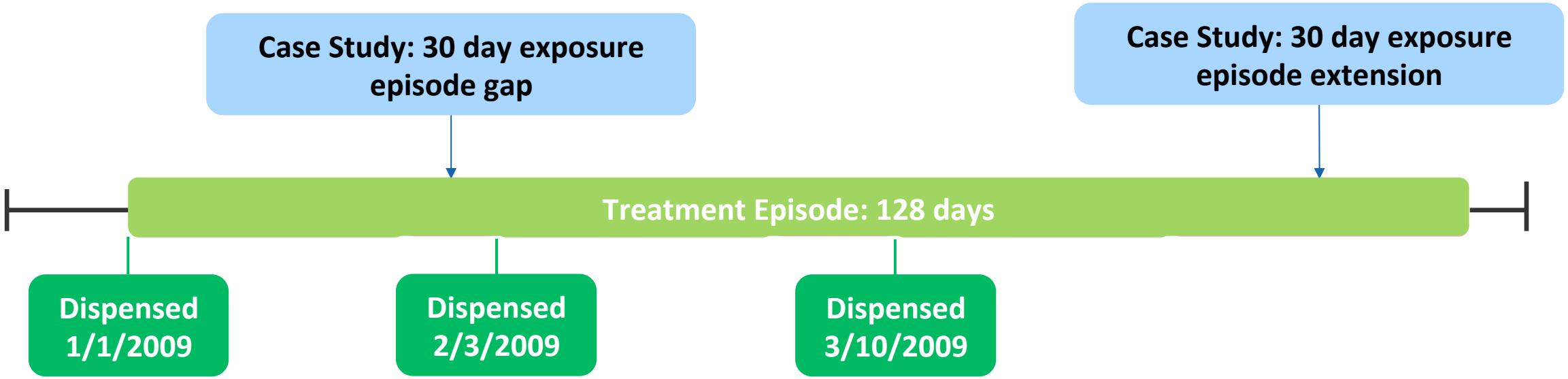
Medical Product Utilization (Type 5)

- Follow patient after "first valid" exposure episode for all available follow-up time in database.
- Output metrics include the number of patients, episodes, dispensings, and days supply; number of episodes by episode number, episode length; number of episode gaps by gap number, gap length.
- Examples:
  - Evaluate utilization patterns of obesity drugs
  - Exploratory study of biosimilar use in Sentinel

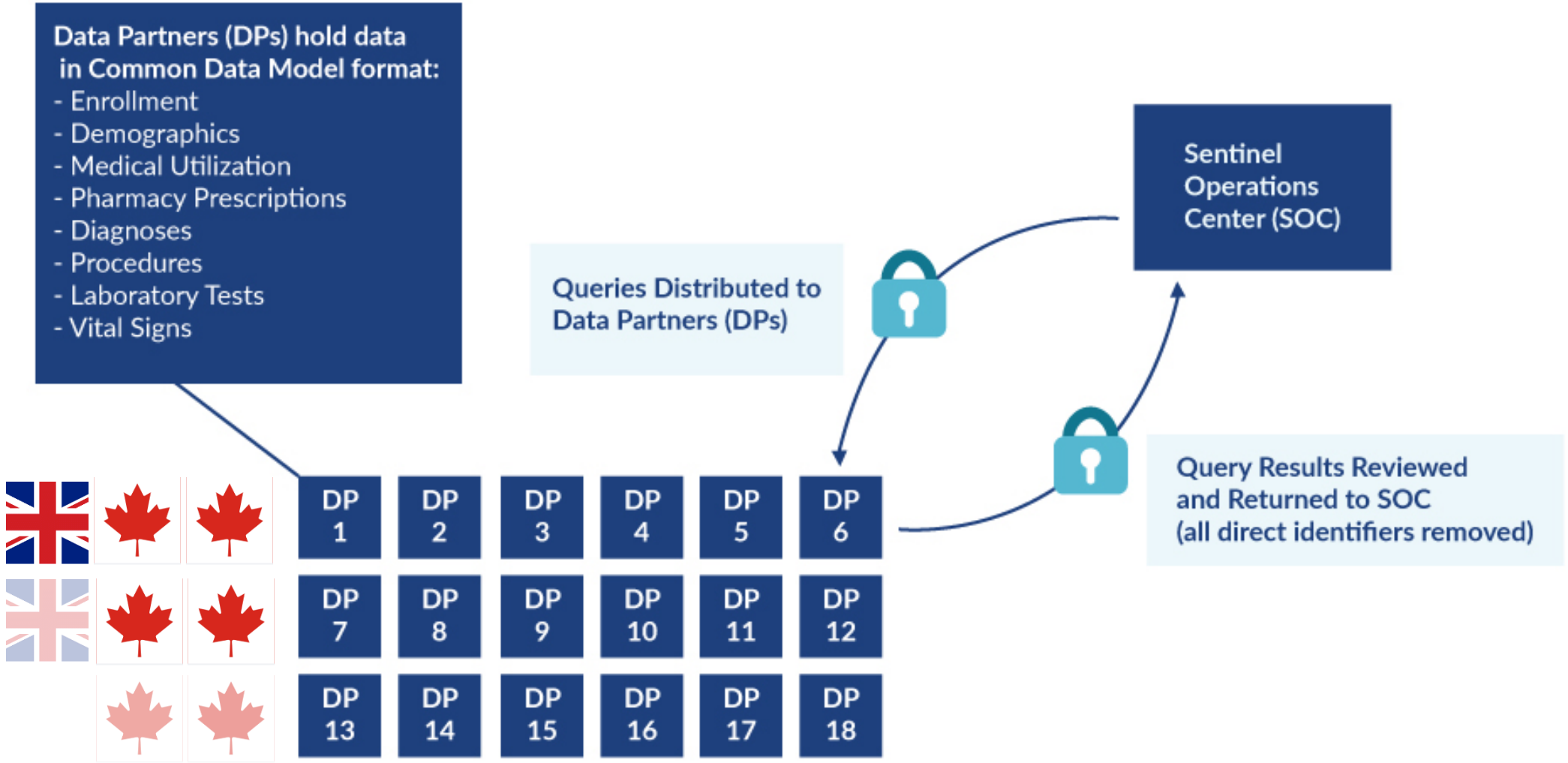
https://www.sentinelinitiative.org/sentinel/surveillance-tools/routine-querying-tools

Developing Time-on-Treatment using Sentinel Tools

1. **Stockpiling** is used to evaluate early refilling behavior, same day dispensings
2. **Gaps** are bridged to deal with late refill behavior
3. **Extension** days are added after any episode gaps have been bridged



Expanded Options for Sentinel as a Distributed Data Network



Quality-Checked Query-Ready Datasets (Solid)
Planned, not yet QC'd Datasets (Transparent)

Data transferred securely

https://www.sentinelinitiative.org/sentinel/sentinels-distributed-database

Generating Country-Stratified Time-On-Treatment Information

- Appropriate to use different measurement parameters based on national practice patterns?
  - Treatment of Overlapping Days Supply, Gaps in Continuous Coverage, etc.
- Analysis techniques to evaluate heterogeneous availability of medications, perhaps to special populations
  - Local, site-specific knowledge is key to successful analysis
  - Methods other than restriction and country-stratification?

Questions?

info@sentinelsystem.org

CANADIAN NETWORK FOR OBSERVATIONAL
DRUG EFFECT STUDIES (CNODES)

Heterogeneity in Drug Data and its Impact in Multi-database Drug Safety Networks: The CNODES Experience

Kristian B. Filion, PhD

Associate Professor and William Dawson Scholar
Departments of Medicine and of Epidemiology, Biostatistics, and Occupational Health
McGill University

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Disclosures

- Salary support award from the *Fonds de recherche Québec – santé* (FRQS; Quebec Foundation for Health Research)
- William Dawson Scholar award from McGill University
- Research grants from Canadian Institutes of Health Research
- No conflicts to disclose

CNODES funding and investigators

Canadian Network for Observational Drug Effect Studies (CNODES), a collaborating center of the Drug Safety and Effectiveness Network (DSEN), is funded by the Canadian Institutes of Health Research (CIHR, Grant #DSE – 146021).

CNODES INVESTIGATORS	
Executive:	Samy Suissa (NPI*), Robert Platt
British Columbia:	Colin Dormuth
Alberta:	Brenda Hemmelgarn
Saskatchewan:	Jacqueline Quail
Manitoba:	Patricia Caetano, Dan Chateau
Ontario:	David Henry, Michael Paterson
Québec:	Jacques LeLorier
Atlantic (NB, NL, NS, PEI):	Adrian Levy, Ingrid Sketris
UK CPRD:	Pierre Ernst, Kristian Filion

*Nominated Principal Investigator

CNODES at a glance

The Canadian Network for Observational Drug Effect Studies (CNODES) uses *population-based administrative healthcare data* to provide *timely responses* to queries for Canadian public stakeholders regarding drug safety and effectiveness

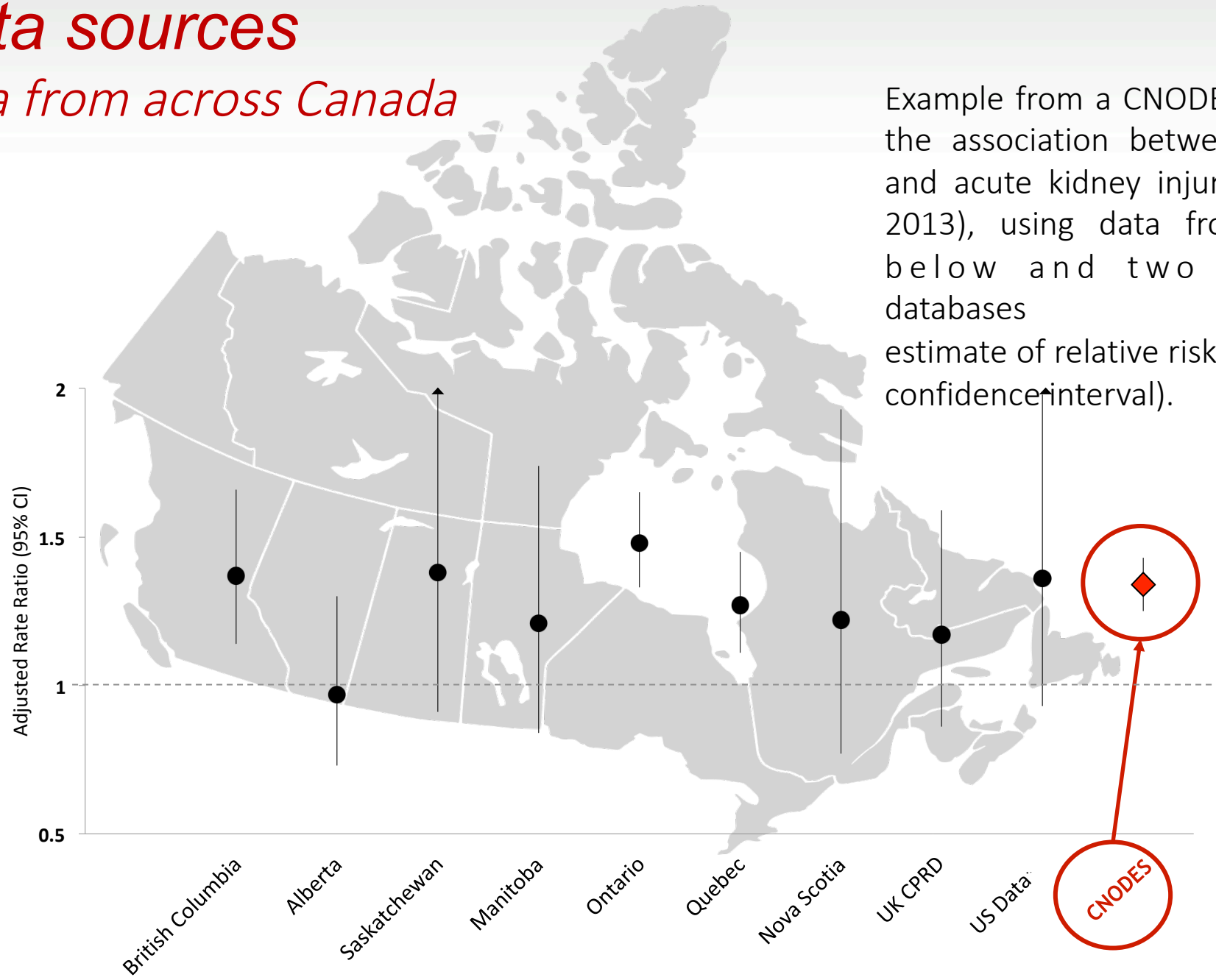
CNODES uses:

- Linked administrative data from *7 provincial* and *2 international* databases
- De-identified administrative health data of *> 100 million people*

Data sources

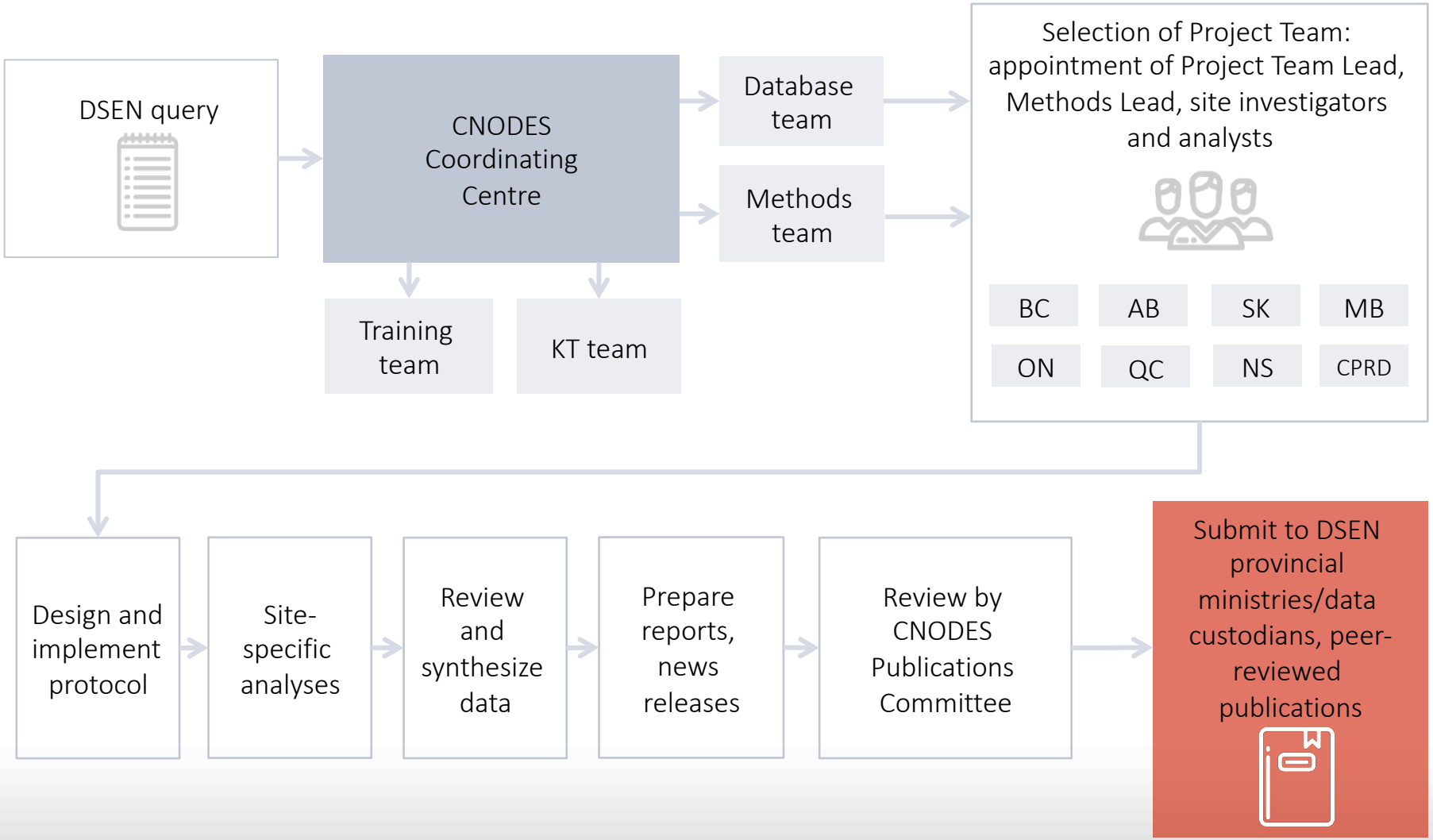
Data from across Canada

Example from a CNODES study examining the association between statin potency and acute kidney injury (Dormuth et al. 2013), using data from the provinces below and two international databases (point estimate of relative risk with 95% confidence interval).



The CNODES process

From query submission to project completion and knowledge translation



Heterogeneity in CNODES drug data

CNODES Site	Drug data	Dispensings captured	Group covered	Coding systems	
				Drug	Class
Alberta[1]	Dispensings	All	≥18 years	DIN	WHO ATC
UK CPRD	Prescriptions	NA	Patients registered in a participating GP	Gemscript	British National Formulary
US MarketScan	Dispensings	Private	All	NDC	AHFS

Key challenge:

Developing scientific protocols and statistical analysis plans that can be implemented in a reproducible manner cross sites with minimal heterogeneity while capturing the nuances of the data available at each site.

[1]Alberta also has access to a second drug database capturing prescriptions for age ≥65 years (1994 onwards).
[2]Saskatchewan also has access to a second drug database capturing all community pharmacy dispensations.
Abbreviations: AHFS, American Hospital Formulary System; DIN, Drug Identification Number; GP, general practice; INN, International Non-proprietary Names; NDC, National Drug Code.

Comparative safety of direct oral anticoagulants and warfarin in venous thromboembolism: multicentre, population based, observational study

Min Jun,[1,2,3] Lisa M Lix,[4] Madeleine Durand,[5] Matt Dahl,[6] J Michael Paterson,[7,8,9] Colin R Dormuth,[10] Pierre Ernst,[11,12] Shenzhen Yao,[13] Christel Renoux,[11,14,15] Hala Tamim,[16,17] Cynthia Wu,[18] Salaheddin M Mahmud,[19] Brenda R Hemmelgarn,[1] for the Canadian Network for Observational Drug Effect Studies (CNODES) Investigators

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Additional material is published online only. To view please visit the journal online.

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http://dx.doi.org/10.1136/bmj.j4323

Accepted: 11 September 2017

ABSTRACT

OBJECTIVE

To determine the safety of direct oral anticoagulant (DOAC) use compared with warfarin use for the treatment of venous thromboembolism.

DESIGN

Retrospective matched cohort study conducted between 1 January 2009 and 31 March 2016.

SETTING

Community based, using healthcare data from six jurisdictions in Canada and the United States.

PARTICIPANTS

59 525 adults (12 489 DOAC users; 47 036 warfarin users) with a new diagnosis of venous DOAC use. No difference was found in the risk of death (pooled hazard ratio 0.99, 0.84 to 1.16) for DOACs compared with warfarin use. There was no evidence of heterogeneity across centres, between patients with and without chronic kidney disease, across age groups, or between male and female patients.

CONCLUSIONS

In this analysis of adults with incident venous thromboembolism, treatment with DOACs, compared with warfarin, was not associated with an increased risk of major bleeding or all cause mortality in the first 90 days of treatment.

TRIAL REGISTRATION

Clinical trials NCT02833987.

Jun et al. BMJ 2017.

Methods

8 databases (planned)

- Alberta, Alberta, Manitoba, Saskatchewan, Ontario, Quebec, Nova Scotia, CPRD, MarketScan

Nova Scotia: Excluded due to small number of events

Study population

- New users of direct oral anticoagulants or warfarin in the 30 days post venous thromboembolism (VTE), matched on age, sex, calendar time, and propensity score

Exposure:

- Intention-to-treat

Outcomes:

- Major bleeding and all-cause mortality within 90 days of initiation

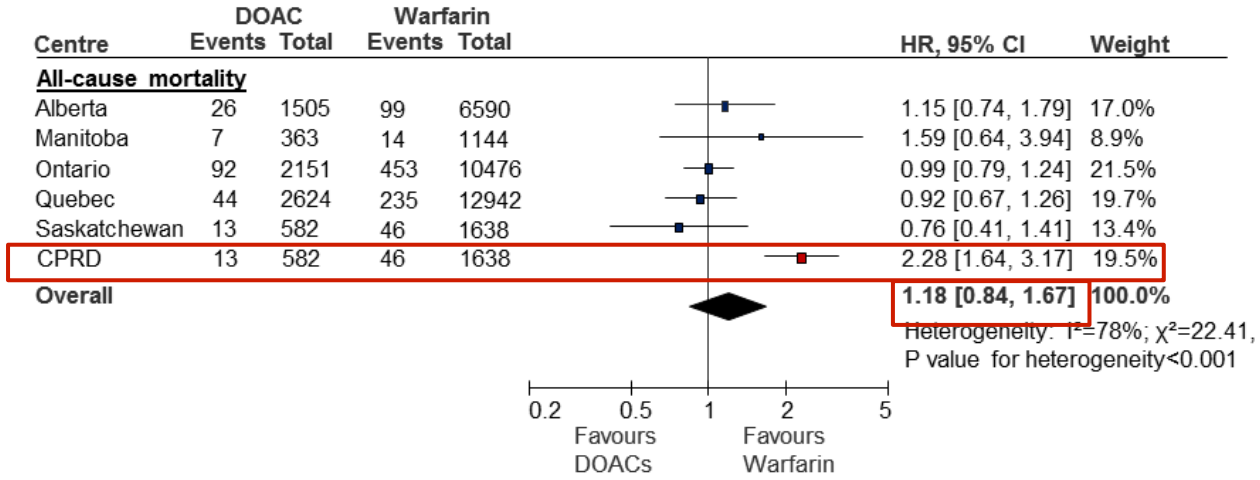
Statistical analysis

- Shared frailty model to account for repeat observations

Jun et al. BMJ 2017.

DOAC vs warfarin among VTE patients

With CPRD



Note: MarketScan was excluded from all-cause mortality analysis due to incomplete capture of events.

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Jun et al. BMJ 2017.

Sources of heterogeneity?

1. Incomplete and differential capture of VTE in CPRD Gold

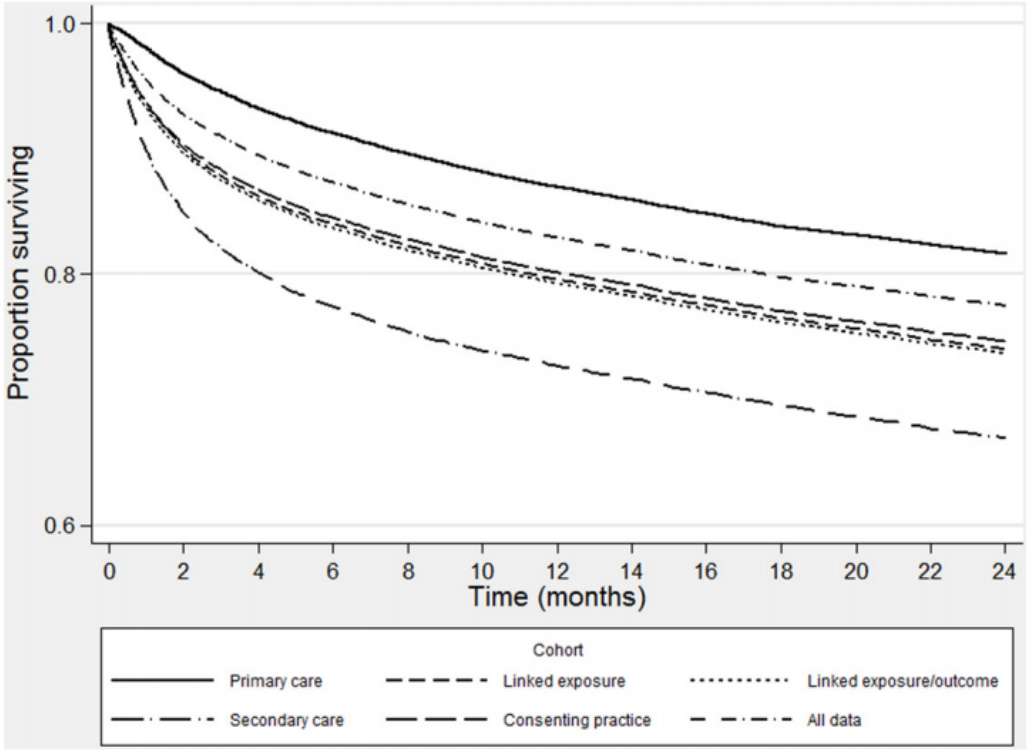


Fig 3. Mortality rate following VTE over time, by cohort.

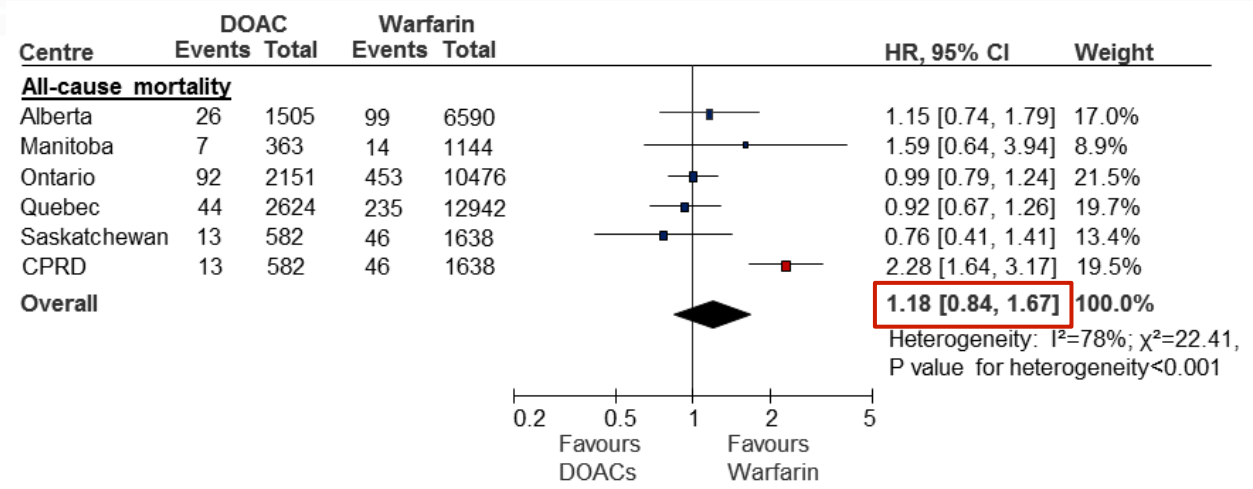
Mortality from venous thromboembolism based on CPRD data are substantially underestimated using the general practice electronic records only (selection bias)

2. Concerns regarding incomplete capture of anticoagulants among VTE patients given 30-day exposure assessment window

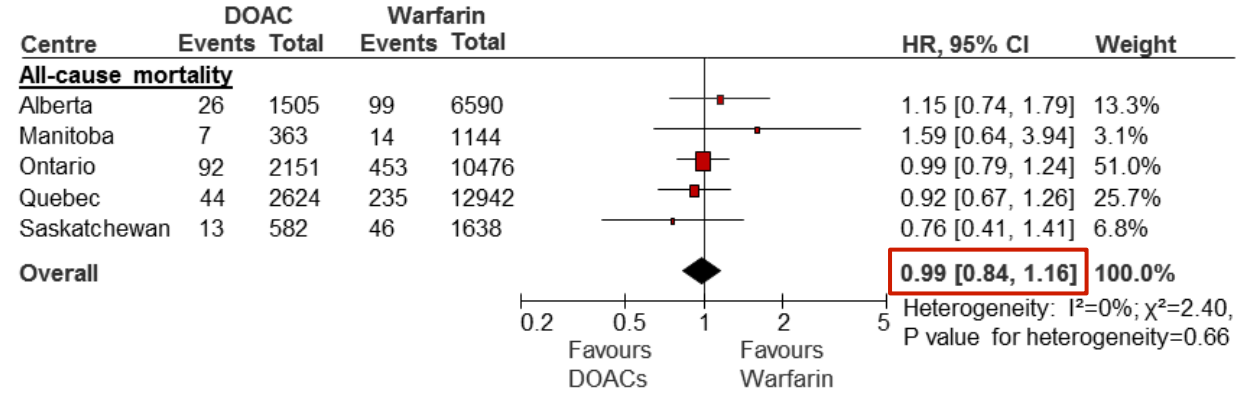
Gallagher et al. Plos One 2016.

DOAC vs warfarin among VTE patients

With CPRD



Without CPRD



Note: MarketScan was excluded from all-cause mortality analysis due to incomplete capture of events.

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CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Jun et al. BMJ 2017.

Gut

ORIGINAL ARTICLE

Proton pump inhibitors and the risk of hospitalisation for community-acquired pneumonia: replicated cohort studies with meta-analysis

Kristian B Filion,[1] Dan Chateau,[2] Laura E Targownik,[3] Andrea Gershon,[4] Madeleine Durand,[5] Hala Tamim,[6] Gary F Teare,[7] Pietro Ravani,[8] Pierre Ernst,[1] Colin R Dormuth,[9] the CNODES Investigators

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/gutjnl-2013-304738).

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ABSTRACT

Objective Previous observational studies suggest that the use of proton pump inhibitors (PPIs) may increase the risk of hospitalisation for community-acquired pneumonia (HCAP). However, the potential presence of confounding and protopathic biases limits the conclusions that can be drawn from these studies. Our objective was, therefore, to examine the risk of HCAP with PPIs prescribed prophylactically in new users of non-steroidal anti-inflammatory drugs (NSAIDs).

Significance of this study

What is already known on this subject?

- Previous observational studies and their meta-analysis have found that proton pump inhibitors are associated with an increased risk of community-acquired pneumonia.
- Potential confounding by gastroesophageal

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Filion et al. Gut 2014.

Methods

7 databases

- Alberta, Manitoba, Ontario, Quebec, Nova Scotia, CPRD, MarketScan

Study population

- New users of non-steroidal anti-inflammatory drugs (NSAIDs)

Outcome:

- Hospitalization for community-acquired pneumonia

Exposure:

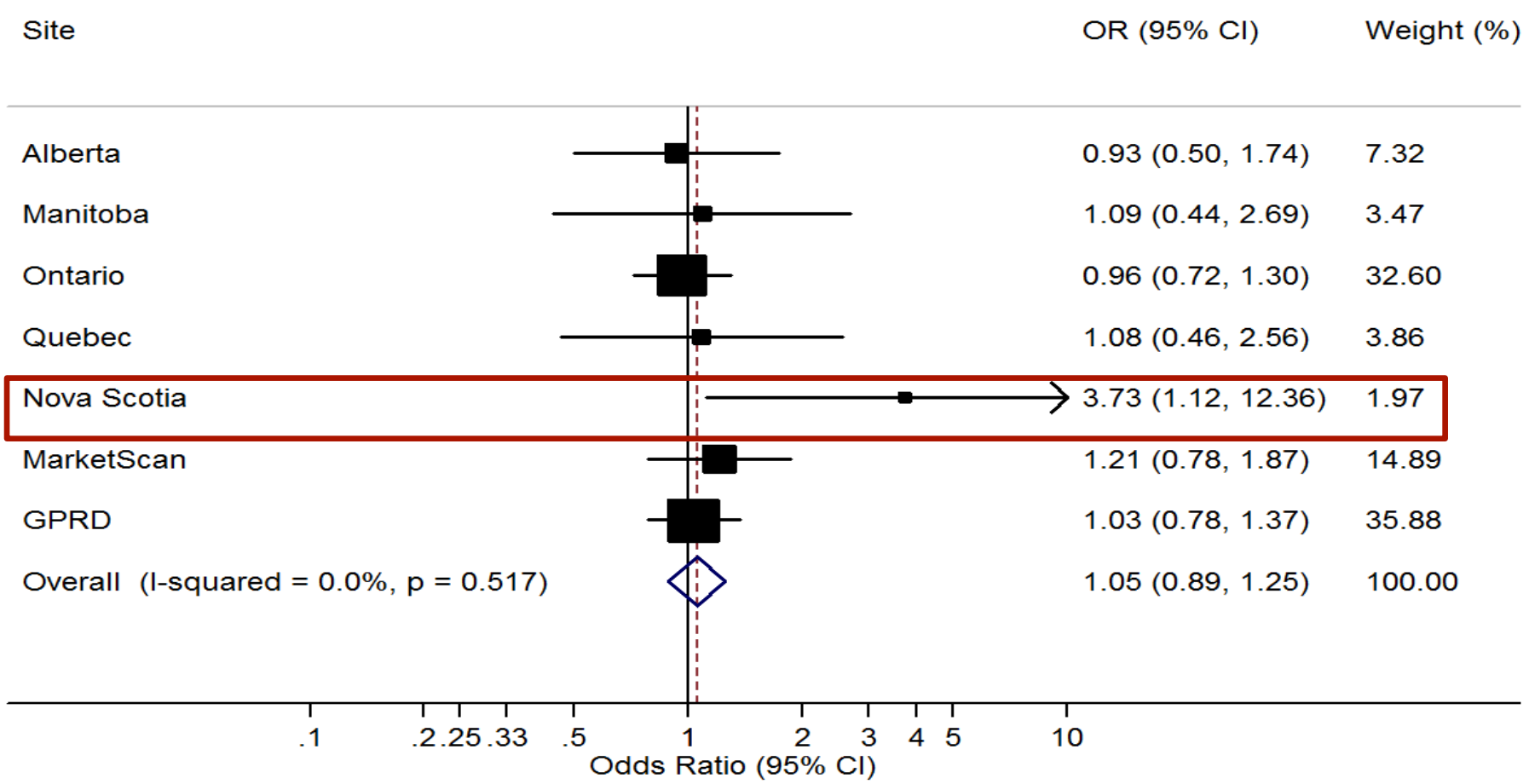
- New PPI on the same day as NSAID prescription vs no PPI

Statistical analysis

- Intention-to-treat analysis
- Follow-up = 6 months
- Logistic regression with high-dimensional propensity scores (HDPS)

Filion et al. Gut 2014.

PPIs and HCAP



CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

Filion et al. Gut 2014.

Confounding by formulary restrictions: fluticasone/salmeterol in Quebec

- Linked administrative health care data from Quebec
- Cohort of new users of fluticasone/salmeterol combination therapy
- Compared respiratory outcomes with 12 months of new user among new users from the liberal period (Sept 1999 to Sept 2003) to those of new users in the restricted period (January 2004 to October 2006)

Table 3. Hazard ratios of hospitalization for respiratory causes, hospitalization for any cause, and all-cause mortality among new users of fluticasone/salmeterol before and after the introduction of formulary restrictions in Quebec, Canada

Period*	Number of events	Number of person years	HR (95%CI) Crude	Age and sex adjusted	Partially adjusted model†	Fully adjusted‡
Hospitalizations for respiratory causes:						
Restricted	1020	3889	1.41 (1.32, 1.51)	1.33 (1.25, 1.42)	1.05 (0.98, 1.12)	0.78 (0.73, 0.83)
Liberal	10 001	53 537	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
Hospitalizations for any cause:						
Restricted	1248	3783	1.19 (1.12, 1.26)	1.13 (1.07, 1.20)	0.96 (0.90, 1.02)	0.82 (0.77, 0.87)
Liberal	14 378	51 490	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)
All-cause mortality:						
Restricted	274	4359	1.40 (1.24, 1.59)	1.28 (1.13, 1.45)	1.10 (0.97, 1.25)	0.97 (0.84, 1.11)
Liberal	2610	58 126	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)	1.0 (Ref)

Filion et al. PDS 2016.

Moving forward:

The study of SGLT2 inhibitors

SGLT2 inhibitors provincial formulary listing

Note: SGLT2 inhibitors are not covered by the public drug plan in British Columbia.

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Comparison of publically vs privately reimbursed users in Manitoba

	DPP-4 inhibitors		SGLT2 inhibitors	
	Public (n = 1,546)	**Private (n = 4,059)**	**Public (n = 1,525)**	**Private (n = 5,990)**
Age (years), mean ± SD	62.0 ± 13.2	57.2 ± 13.4	59.8 ± 12.0	56.8 ± 11.7
≥66, n (%)	622 (40.2)	1,036 (25.6)	487 (31.9)	1,449 (24.3)
Females, n (%)	753 (48.7)	1,933 (47.6)	647 (42.4)	2,661 (44.4)
Income quintile, n (%)				
1st (lowest)	325 (21.0)			
2nd	336 (21.7)	1,178 (29.0)	310 (20.3)	1,288 (21.5)
3rd	343 (22.2)	929 (22.9)	339 (22.2)	1,291 (21.6)
4th	284 (18.4)	723 (17.8)	334 (21.9)	1,183 (19.7)
5th (highest)	236 (15.3)	661 (16.3)	298 (19.5)	1,170 (19.5)
Missing	22 (1.4)	545 (13.4)	230 (15.1)	1,041 (17.4)
Calendar year of cohort entry, n (%)				
2016	694 (44.9)	1,872 (46.1)	386 (25.3)	3,518 (58.7)
2017	676 (43.7)	1,740 (42.9)	855 (56.1)	1,974 (33.0)
2018	176 (11.4)	447 (11.0)	284 (18.6)	498 (8.3)

Comparison of publically vs privately reimbursed users in Manitoba

	DPP-4 inhibitors		SGLT2 inhibitors	
	Public (n = 1,546)	**Private (n = 4,059)**	**Public (n = 1,525)**	**Private (n = 5,990)**
Diabetes duration (years), mean ± SD	11.8 ± 7.8	11.2 ± 8.0	11.5 ± 7.2	11.7 ± 7.7
Comorbidities, n (%)				
Myocardial infarction	14 (0.9)	21 (0.5)	15 (1.0)	52 (0.9)
Heart failure	10 (0.6)	25 (0.6)	12 (0.8)	25 (0.4)
Coronary artery disease	304 (19.7)	566 (13.9)	331 (21.7)	1,046 (17.5)
Dyslipidemia	392 (25.4)	859 (21.2)	406 (26.6)	1,434 (23.9)
Hypertension	1,214 (78.5)	2,712 (66.8)	1,185 (77.7)	4,241 (70.8)
Medications, n (%)				
Metformin	1,351 (87.4)	3,379 (83.2)	1,391 (91.2)	5,219 (87.1)
Sulfonylureas	1,185 (76.6)	2,740 (67.5)	1,211 (79.4)	3,646 (60.9)
Insulin	90 (5.8)	634 (15.6)	115 (7.5)	1,535 (25.6)
DPP-4 inhibitors	–	–	435 (28.5)	1,589 (26.5)
SGLT2 inhibitors	288 (18.6)	478 (11.8)	–	–
No. non-antidiabetic drugs, mean ± SD	7.6 ± 4.9	7.7 ± 5.4	7.4 ± 4.6	7.3 ± 5.0

Conclusions

- *Heterogeneity* in the measurement of prescription drug data represents *a key challenge* to the conduct of multi-jurisdictional drug safety studies.
- CNODES has traditionally relied on *exclusion to minimize the impact* of such heterogeneity, both in terms of which sites participate in a given study and in terms of calendar time periods included in a given study.
- There remains *a need to develop* and apply alternative *methodological approaches* to address such heterogeneity. Such approaches would facilitate the *triangulation* of results and potential *adjustment* for sources of heterogeneity in the measurement of prescription drug data as we move to increasingly international collaborations across networks.

Thank you

Visit us at www.cnodes.ca

CNODES
CANADIAN NETWORK FOR OBSERVATIONAL DRUG EFFECT STUDIES

kristian.filion@mcgill.ca

CIHR IRSC

Medicines & Healthcare products Regulatory Agency

CPRD

Prescribing data formatted to the SCDM

Dr Achim Wolf, Senior Researcher

NHS National Institute for Health Research

Disclosures

Full-time employee of Clinical Practice Research Datalink (CPRD), a division of the UK Medicines and Healthcare products Regulatory Agency (MHRA).

Views expressed are my own and do not represent the official position of either the CPRD or the MHRA.

Honorary Researcher at the Department of Psychiatry, University of Oxford

UK Healthcare System

The National Health Service (NHS)

Launched 70 years ago

Free at point of use

GPs: primary point of contact for non-emergency (93% consultations)

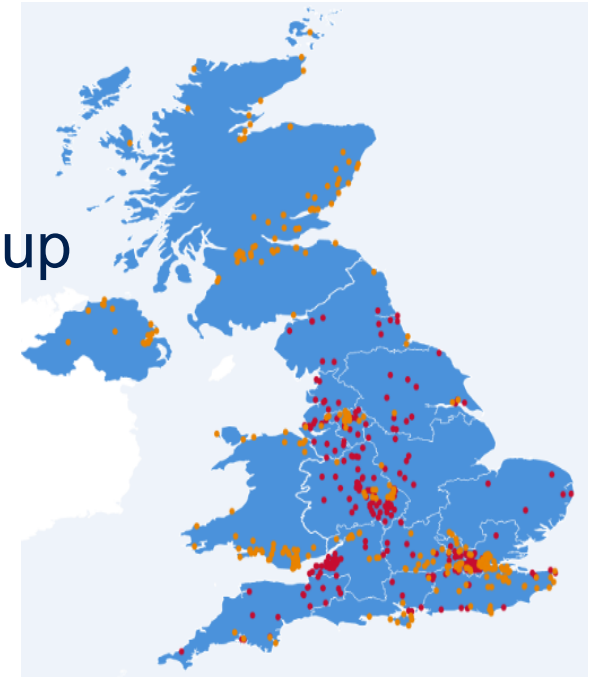
- ‘Gatekeepers’ – each patient registered with one GP
- Lifetime medical record travels with individual
- Unique NHS number for each patient

GP Medical Records

- Patient data routinely recorded onto computers
  - Patient demographics
  - Signs, symptoms and diagnoses
  - Primary care prescriptions (drugs and devices)
  - Immunisations
  - Test results
  - Referrals to specialist / secondary care
  - Feedback from other care settings
  - Lifestyle information
    - BMI, smoking, alcohol, exercise etc.

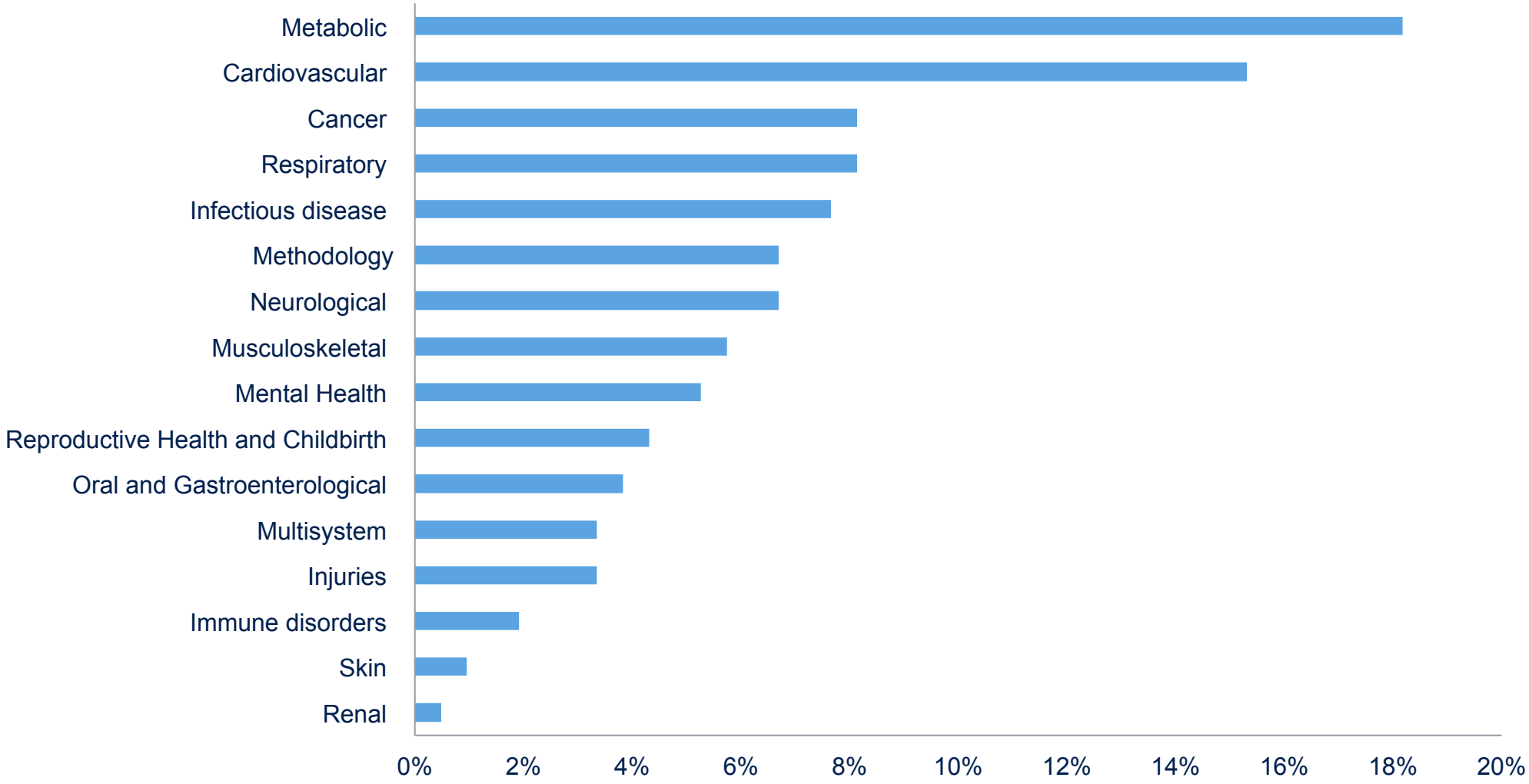
CPRD Population Coverage

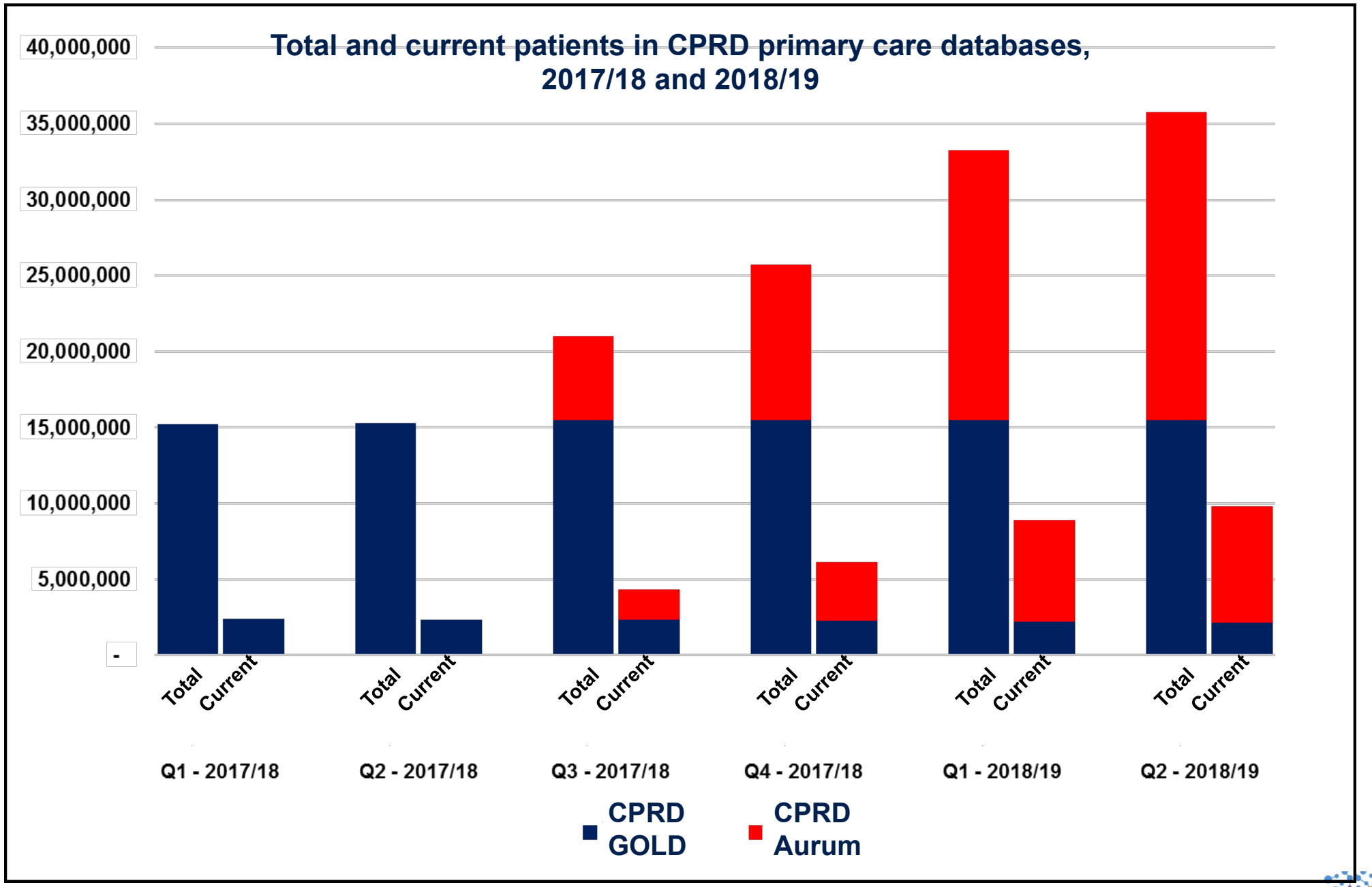
- Over 40 million total patient lives on CPRD databases
- 11 million currently registered patients – 17% of UK population
- Near real-time data collection – daily updates
- Median follow up time of 10 years – some life-long follow up
- Secondary care and mortality linked data sources



CPRD

CPRD research output by disease areas




Total and current patients in CPRD primary care databases, 2017/18 and 2018/19
40,000,000
35,000,000
30,000,000
25,000,000
20,000,000
15,000,000
10,000,000
5,000,000
-
Total
Current
Q1 - 2017/18
Q2 - 2017/18
Q3 - 2017/18
Q4 - 2017/18
Q1 - 2018/19
Q2 - 2018/19
CPRD GOLD
CPRD Aurum

CPRD GOLD & CPRD Aurum

August 2019 figures

	CPRD GOLD	CPRD Aurum
Software system	Vision	EMIS
Patients [practices]		
All:	17.5M [840]	23.8M [895]
Current:	2.9M [347]	8.4M [863]
Linked (Set 17):	8.9M	20.1M
Follow up (y): median [IQR]		
All patients:	5.6 [2.0 - 13.2]	4.7 [1.8 – 12.0]
Current patients:	12.3 [4.5 - 24.0]	9.2 [3.4 – 20.6]
Regional distribution of current practices (%)		
England:	100 (29%)	863 (100%)
Northern Ireland:	32 (9%)	-
Scotland:	125 (36%)	-
Wales:	90 (26%)	-

CPRD

CPRD GOLD & CPRD Aurum

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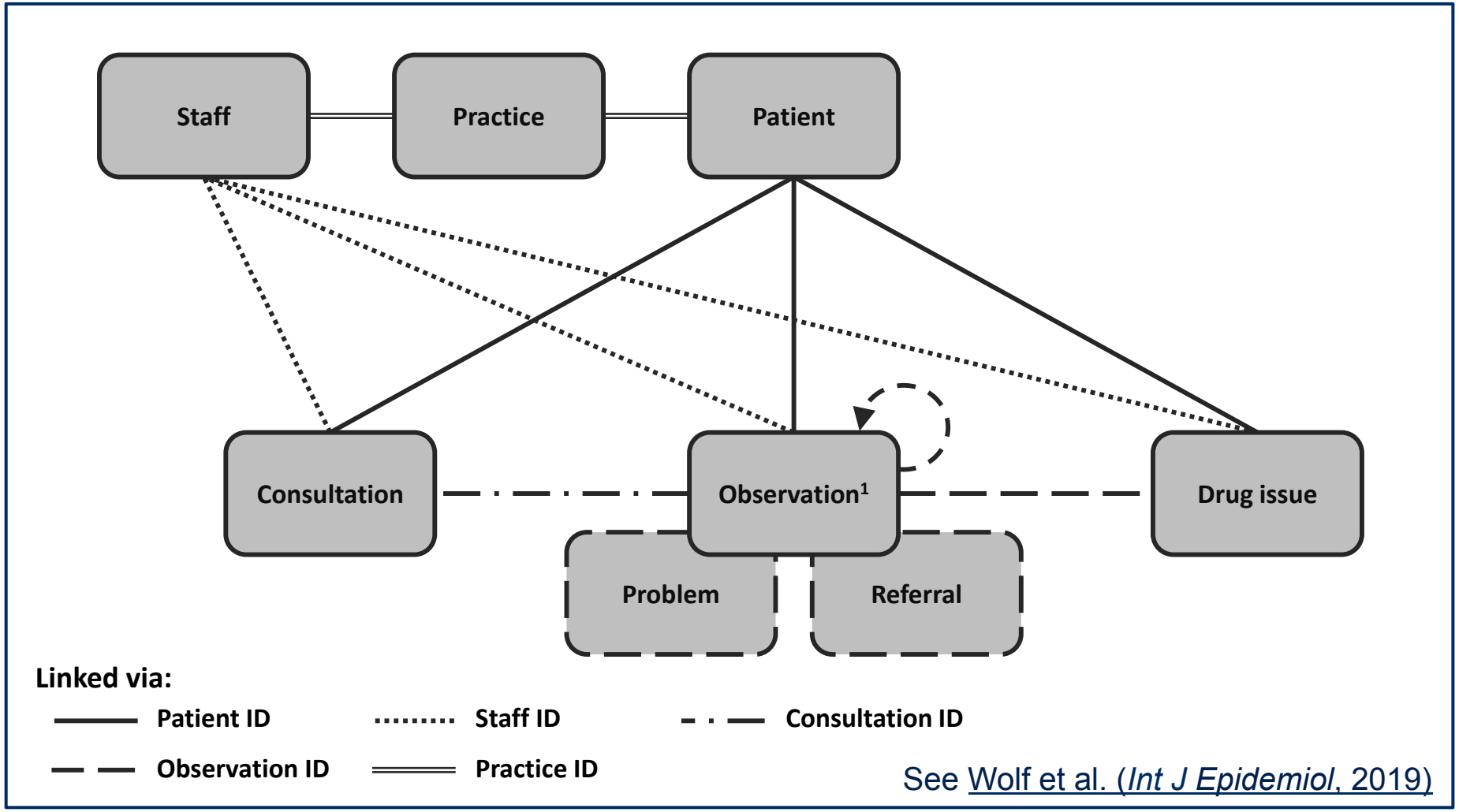
CPRD

CPRD Aurum

Structure



See Wolf et al. (*Int J Epidemiol*, 2019)

Administrative Data

Enrollment	Demographic	Dispensing	Encounter	Diagnosis	Procedure
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth date	Dispensing Date	Service Date(s)	Service date(s)	Service Date(s)
Drug Coverage	Sex	National Drug Code (NDC)	Encounter ID	Encounter ID	Encounter ID
Medical Coverage	Zip code	Days Supply	Encounter Type and Provider	Encounter Type and Provider	Encounter Type and Provider
Medical Record Availability	Etc.	Amount Dispensed	Facility	Diagnosis Code & Type	Procedure Code & Type
			Etc.	Principle Discharge Diagnosis	Etc.

Clinical Data

Lab Result	Vital Signs
Patient ID	Patient ID
Result & Specimen Collection Dates	Measurement Date & Time
Test Type, Immediacy & Location	Height & Weight
Logical Observation Identifiers Names and Codes (LOINC®)	Diastolic & Systolic BP
Etc.	Tobacco Use & Type
	Etc.

Registry Data

Death	Cause of Death
Patient ID	Patient ID
Death Date	Cause of Death
Source	Source
Confidence	Confidence
Etc.	Etc.

Inpatient Data

Inpatient Pharmacy	Inpatient Transfusion
Patient ID	Patient ID
Administration Date & Time	Administration Start & End Date & Time
Encounter ID	Encounter ID
National Drug Code (NDC)	Transfusion Administration ID
Route	Transfusion Product Code
Dose	Blood Type
Etc.	Etc.

Mother-Infant Linkage Data

Mother-Infant Linkage
Mother ID
Mother Birth Date
Encounter ID & Type
Admission & Discharge Date
Child ID
Child Birth Date
Mother-Infant Match Method
Etc.

CPRD / SCDM Proof Of Concept

Subset of CPRD Aurum ('MVP'):

- 13 GP practices
- Ca. 500k patients (current and historic)

Utility:

- Drugs and conditions
- Procedures and diagnoses
- Prescribing rather than dispensing

Mapping:

- Patient data during their registration period at the practice

Administrative Data

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Administrative Data

Enrollment	Demographic	Prescribing	Encounter	Diagnosis	Procedure
Patient ID	Patient ID	Patient ID	Patient ID	Patient ID	Patient ID
Enrollment Start & End Dates	Birth date	Dispensing Date	Service Date(s)	Service date(s)	Service Date(s)
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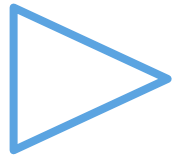
SCDM Mapping

New code type – SNOMED UK (SK)

- SNOMED
  - SNOMED CT Core
  - SNOMED CT UK Extension



Diagn
Proce

Encounter

- No analogue in CPRD Aurum

Enrolment

- MedCov – Ambulatory added

SCDM Table	Records
Enrolment	511,412
Demographic	511,412
Death	24,679
Encounter	21,920,166
Diagnosis	23,520,028
Procedure	10,533,081
Prescribing	36,130,122

Antidiabetic query

Original query (WP092)

Population: 18+ with registration from Jan 2008 to Jan 2018

Exposure: Non-insulin antidiabetic drugs

albiglutide, alogliptin, canagliflozin, dapagliflozin, dulaglutide, empagliflozin, exenatide, glimepiride, glipizide, glyburide, linagliptin, liraglutide, metformin, pioglitazone, saxagliptin, sitagliptin

Treatment Episode creation: Incident dispensing

183-days prior exposure-free follow-up. 10-day gap allowable.

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Results: Dispensing (Patients)

	DPs (17 sites)	CPRD MVP
Metformin	71,316,729 (6,502,864)	123,389 (4,463)

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All sulphonylureas?		

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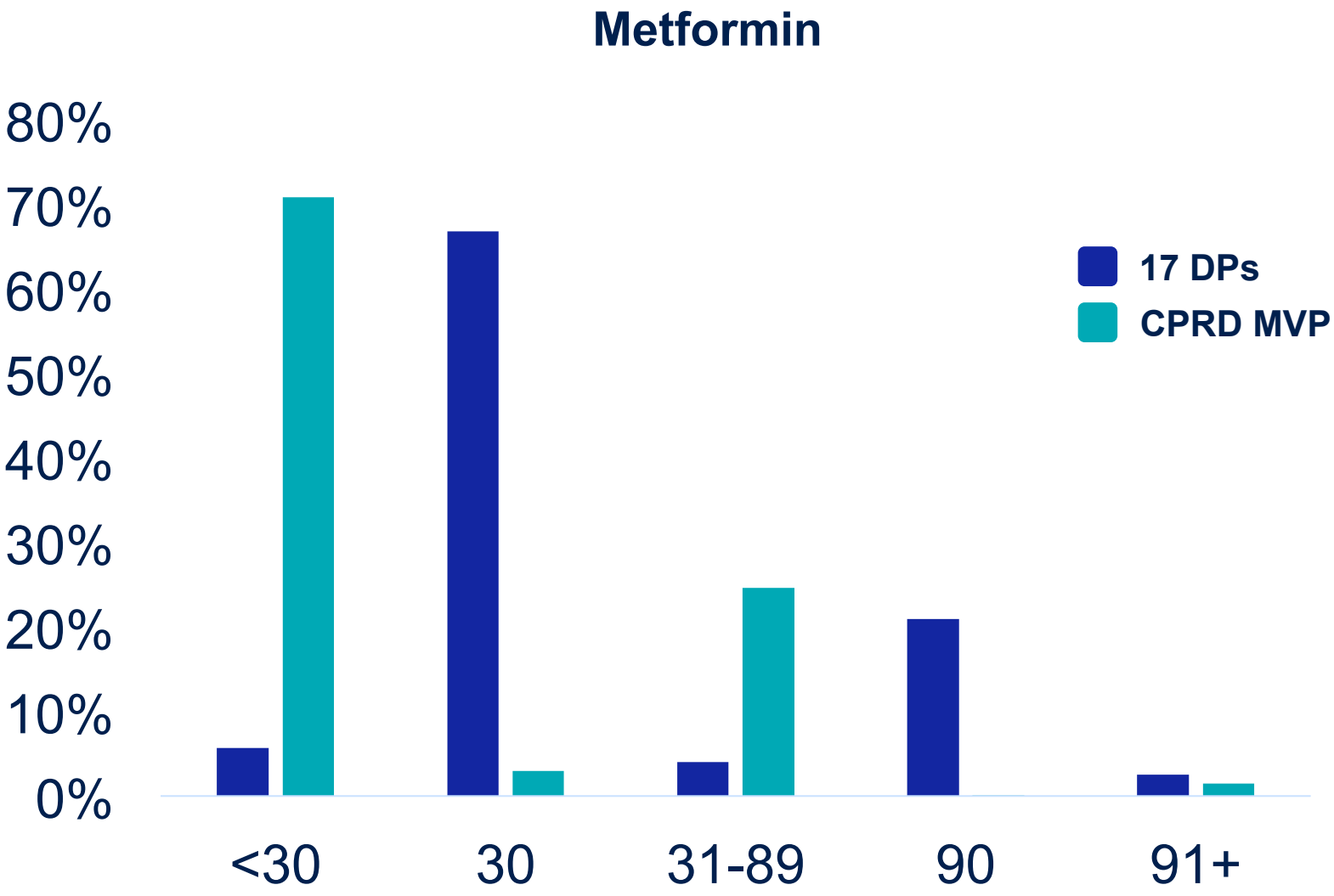
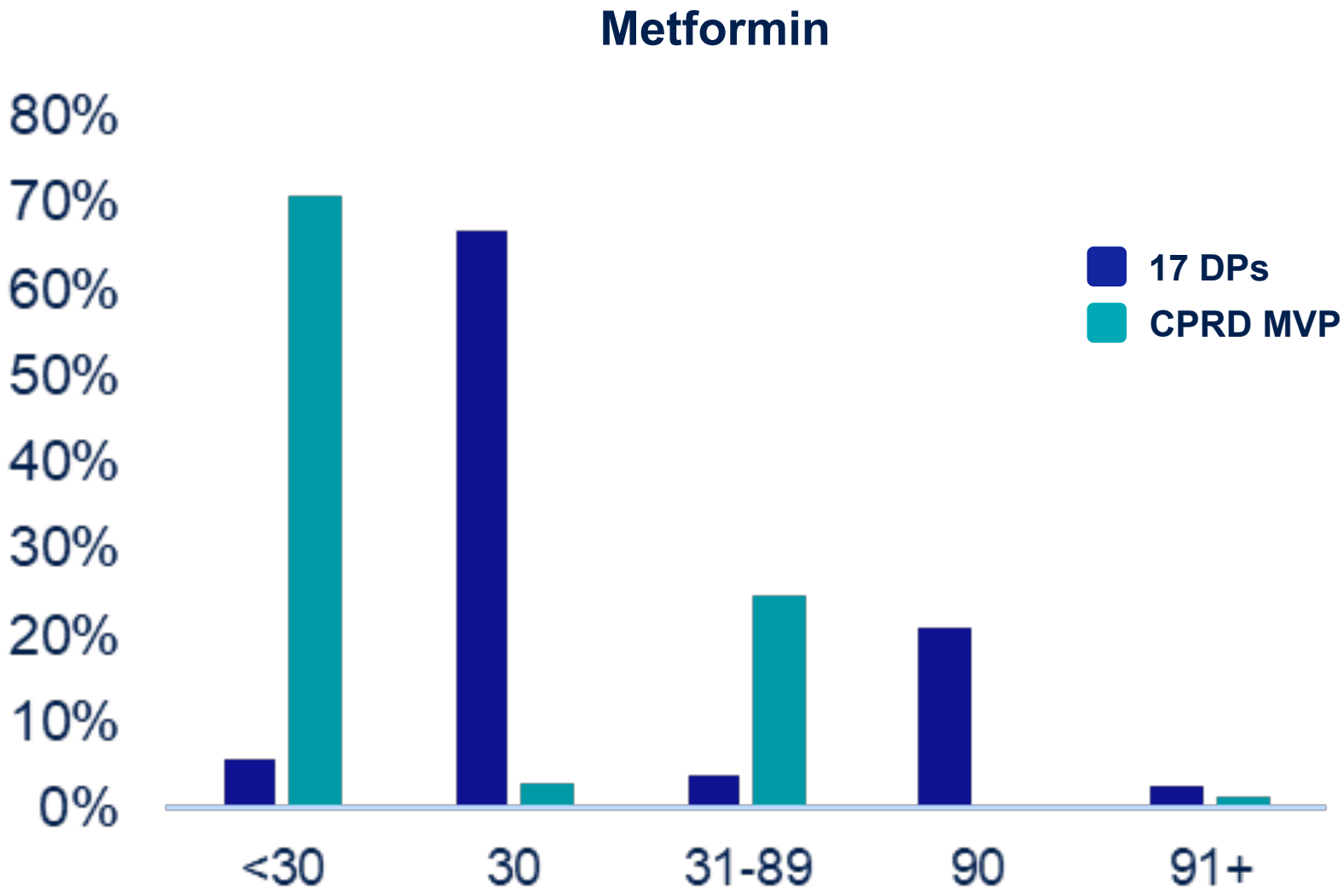
Gliclazide	0 (0)	58,093 (2,027)
All sulphonylureas?	-	61,111 (2,138)

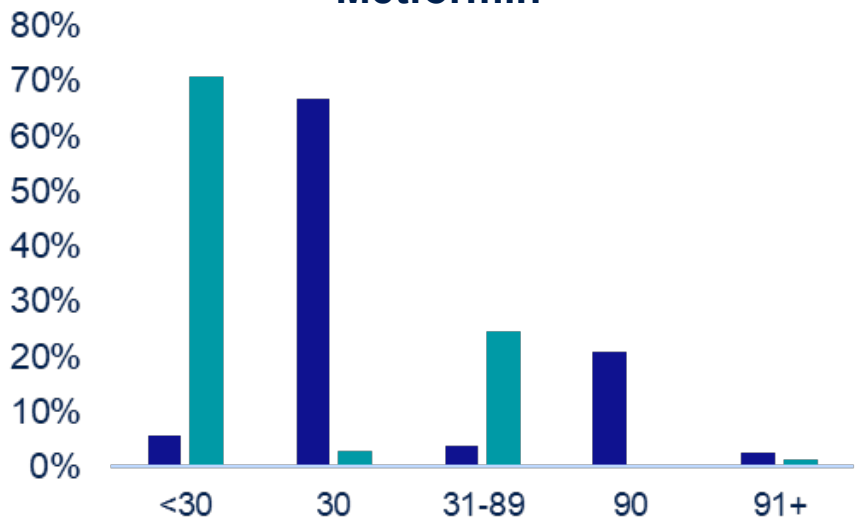
Days prescribed



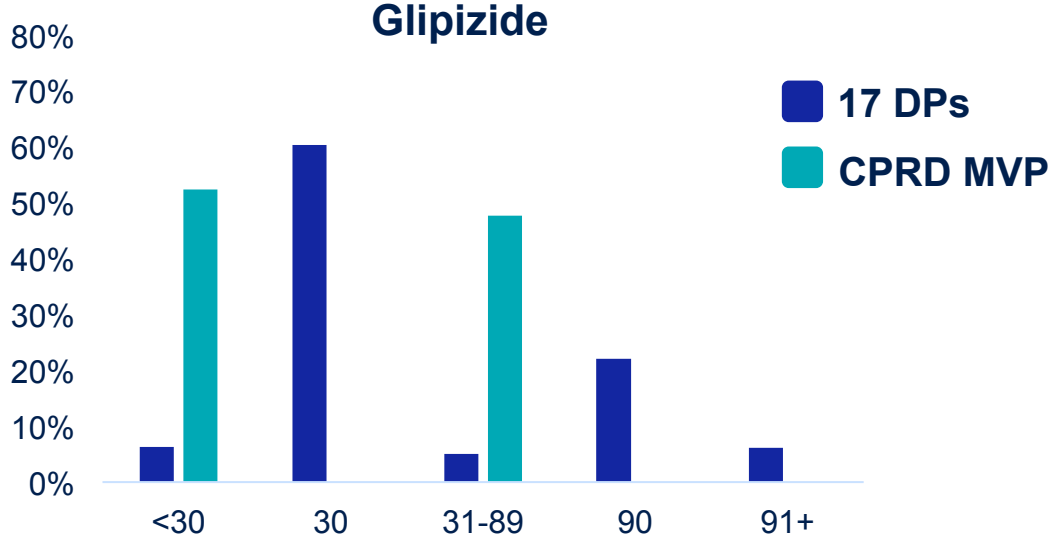
Days prescribed



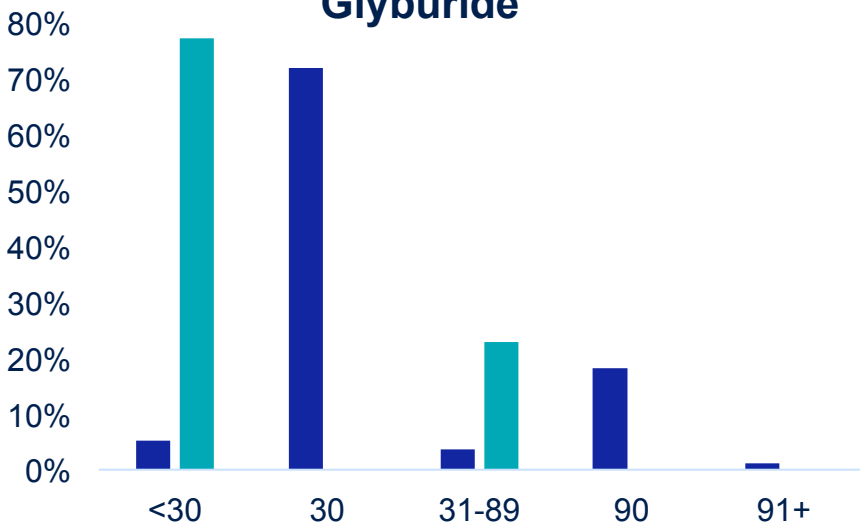
Metformin



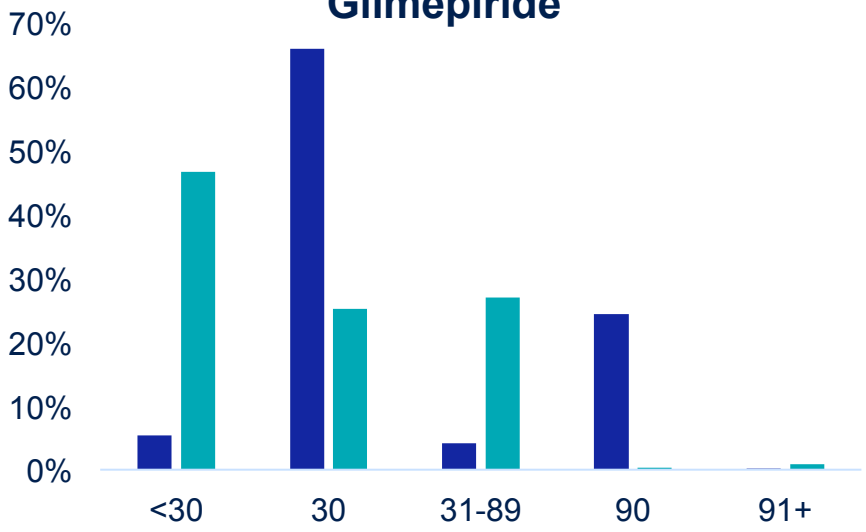
Glipizide



Glyburide

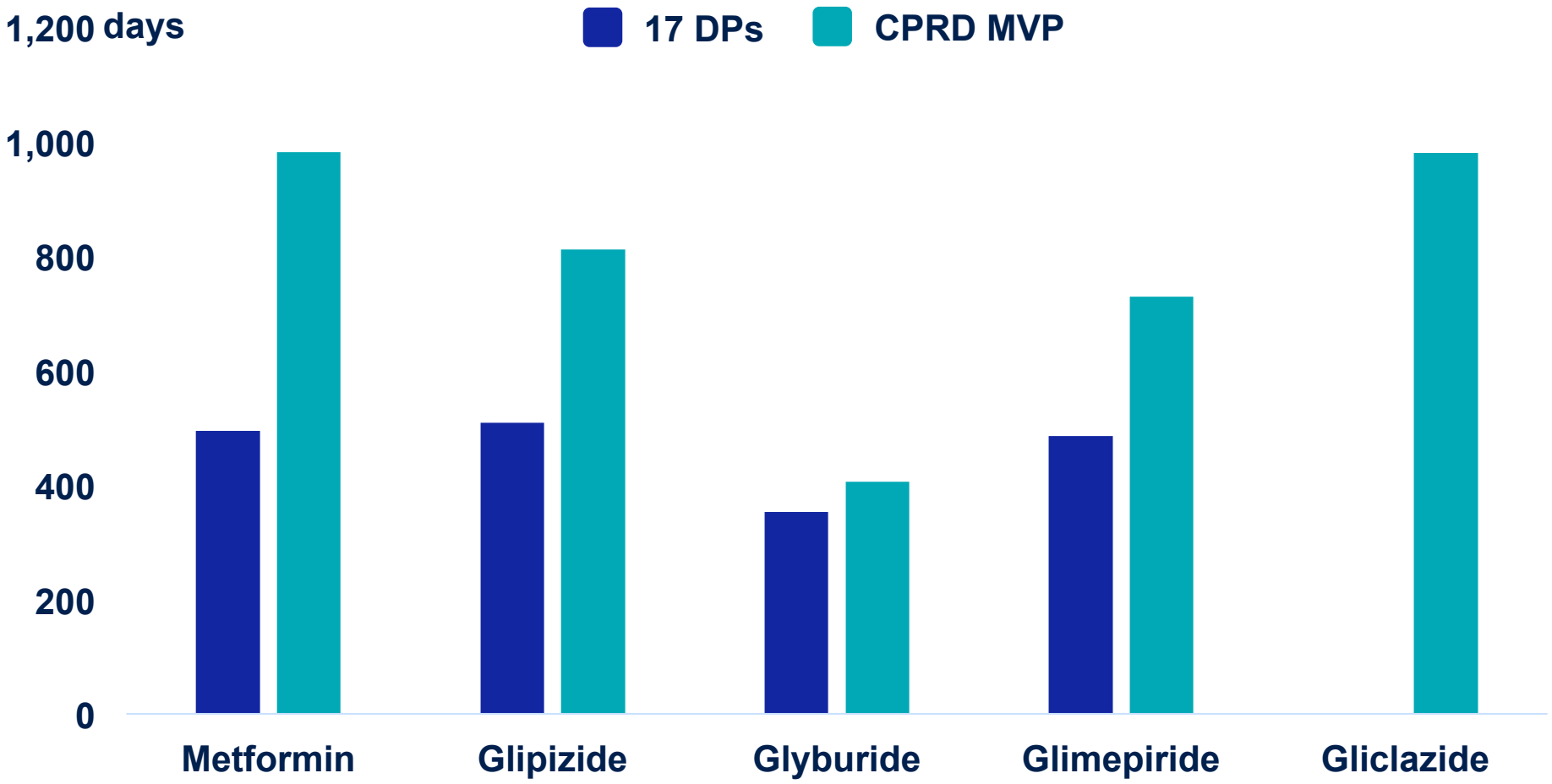


Glimepiride



CPRD

Cumulative exposure duration



Key differences

FIRST LINE TREATMENT

NHS 28-DAY PRESCRIBING POLICY

EXPOSURE/ FOLLOW-UP

PRESCRIBING VS. DISPENSING

On the horizon…

Historical data from before a patient's registration start date

Additional tables:

- Vital Signs, lab values, referrals, problems

Scaling up

- Storage, processing
- Update frequency
- CPRD GOLD

Linkages

- Official death record, secondary care

achim.wolf@mhra.gov.uk

enquiries@cprd.com

The PCORnet Antibiotics and Childhood Growth Study: Prescribing vs. Dispensing

Kevin Haynes, PharmD, MSCE
Vinit Nair, PharmD, MS
Jason Block, MD, MPH
L. Charles Bailey, MD, PhD
Pi-I Debby Lin, ScD

pcornet℠ | The National Patient-Centered Clinical Research Network

Outline

- Short Pecha Kucha Image Presentation of Prescribing vs. Dispensing
  - https://www.pechakucha.com 20slidesx20s/slide (we'll do 7x20s)
- Brief PCORnet Overview
- Overlap of Pediatric Antibiotic Study between Clinical Data Research Networks and Health Plan Research Networks

Disclosures

- Employee of HealthCore, a subsidiary of Anthem
- Funding from PCORI, FDA Sentinel, NIH

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The Children's Hospital of Philadelphia
LEFT TURN SIGNAL
NO TURN ON RED
RIGHT TURN SIGNAL
Civic Center Bl
34th St
34th St
Civic Center Bl
Convention Av
BEGIN ONE WAY
Hospital Entrance
Parking

AccuMed EHR - User: WelbyM Role: Doctor, on PETERM6 using MU2.MU - Internet Explorer

AccuMed™ | Home | Schedule | Referrals | Patient | Messaging | Reports | Admin | Logout

Matulich,Kylie #100233- Female, DOB 01/17/2003, Age 14

> Patient

Patient

- Chart View
  - Patient Search
  - Demographics
  - Treatment Plan
  - Indiv Recovery Plan
  - Document Archival
  - Vitals
  - Educational Materials
  - HIE
- Recent Charts
- Histories
- Quick Links

Appointments

Appointment	Appt Time	Service	Provider	Dur	Status Desc
03/20/2017	02:30 PM	0264	1	15	Not Seen
03/20/2017	10:00 AM	Office Visit 99201	AJ	45	Not Seen

Patient Assessments

PHQ-9 Patient Health Questionnaire (PrimaryCare) Edit Print

▲ 92.00% | Current Score: 2 | Minimal Depression

Documents

Encounter Date	Encounter Name	Active User	EncId
03/29/2017	gVitals	WelbyM	7641

Immunization

Vaccine Date	Vaccine Name

No data to display

Lab Orders

Due Date	has_results	Account	Lab ID

No data to display

Alerts

Subject	Message	Type
System Alert	Diastolic is 90+, monitor for High BP.	ASSIGNED

Problem List

Diag Code	Problem	Category
311	Depressive disorder, not elsewhere classified	ICD9

Medication

Prescribing Date	Drug Name	Notes	Prescribing User
10/18/2010 11:27AM	Ventolin HFA		WelbyM
04/27/2010 10:20AM	Proventil HFA		WelbyM

Vitals

Date	Height	Weight	BMI	BP Systolic	BP Diastolic	Temperature	Enc Id
03/29/2017	72.00	180.00	24.41	110	90	98.60	7641
10/18/2010	72.00	220.00	29.83	110	90	98.60	3350

Allergies

Allergy Name	Reaction	Severity

No data to display

Build No. : 12.10.419.68

100%

FOR _____

ADDRESS _____ DATE _____

℞

REFILL _____ TIMES

_____ M.D. _____ M.D.

DO NOT SUBSTITUTE SUBSTITUTION PERMISSIBLE

DEA NO. _____ _____

ADDRESS

BioRx Labs 1-888-550-5452 FORM NO. PD5000


cvs/pharmacy
Photo
Drive-Thru Pharmacy
Beauty
MoneyGram
cvs/pharmacy
Photo
Drive-Thru Pharmacy
Beauty
pharmacy
photo
beauty

Blue Cross Blue Shield

Enrollee Name
FIRST M LASTNAME JR

Enrollee ID
DZW920000000

Issuer (80840)
9101003777

RxBIN 004336

RxGrp RX4655

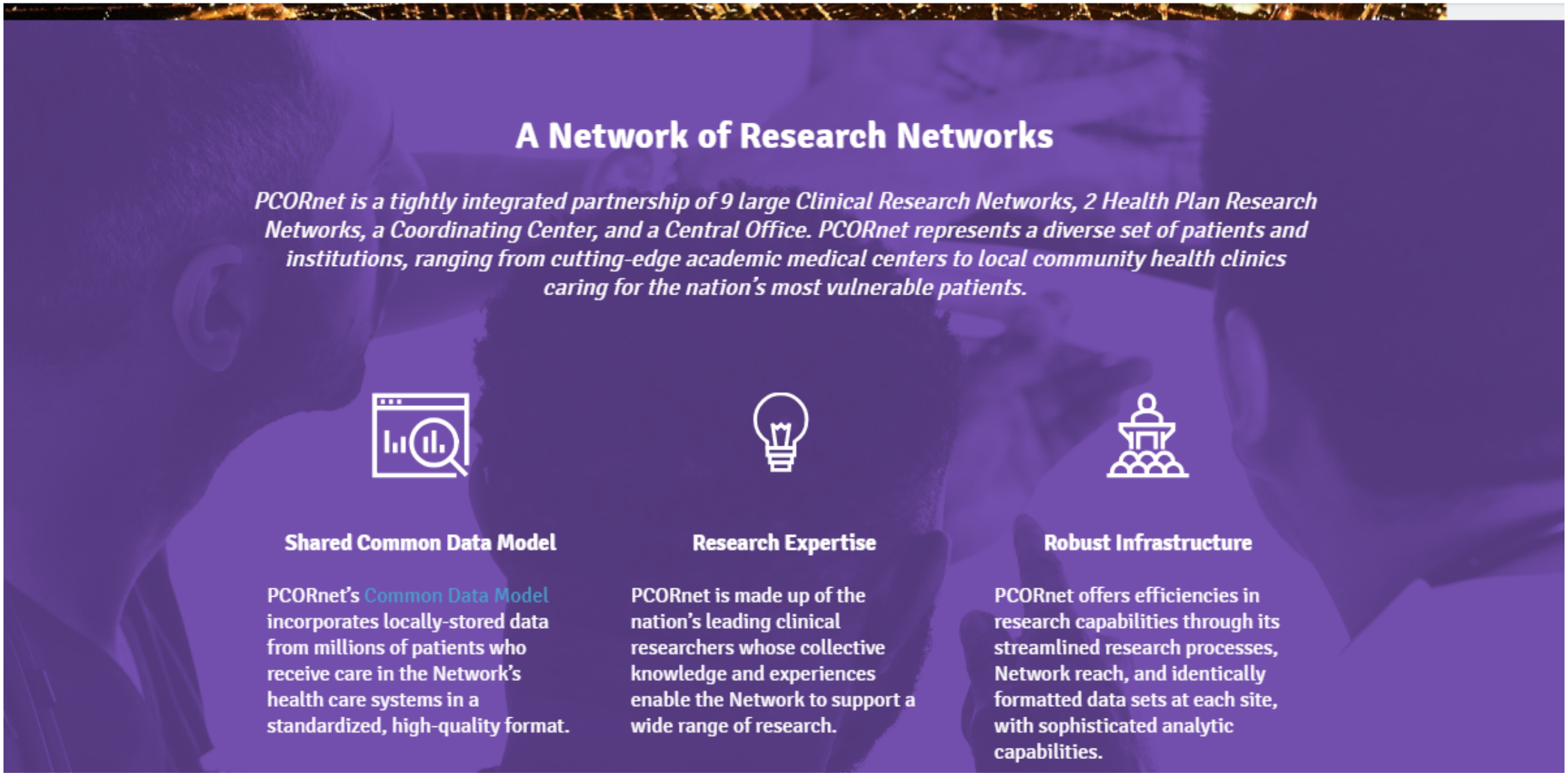
Blue Dental™ smile, you're covered

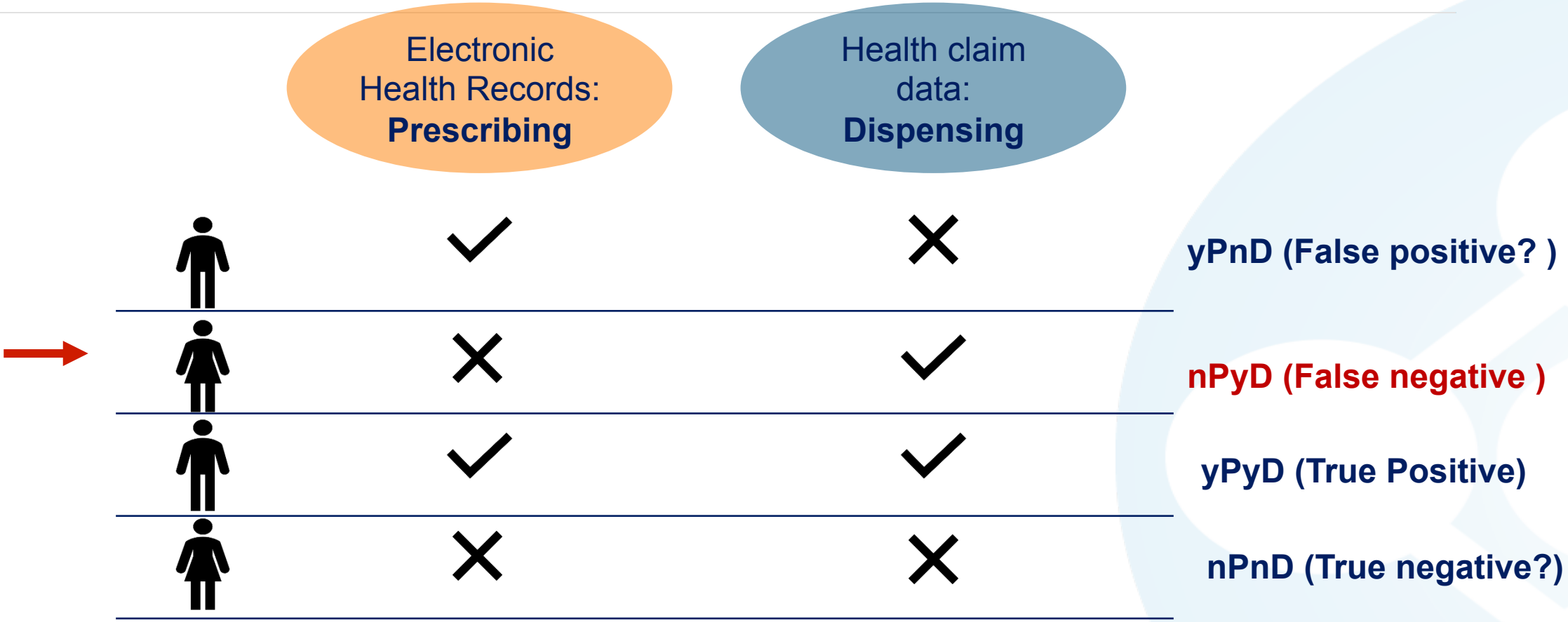
Blue Vision℠

℞


Rx Pharmacy
321 Anywhere Street
Anytown, US 11111
0060023-08291
JOHN SMITH
TAKE ONE CAPSULE BY MOUTH THREE TIMES DAILY FOR 10 DAYS UNTIL ALL TAKEN
ANTIBIOTIC 500MG
Qty 30
MFG
NO REFILLS - DR. AUTHORIZATION
USE BEFORE
Rx Pharmacy
0060023-08291
JOHN SMITH
Rx Pharmacy
0060023-08291
JOHN SMITH

www.pcornet.org




Electronic Health Records: **Prescribing**
Health claim data: **Dispensing**
yPnD (False positive?)
nPyD (False negative)
yPyD (True Positive)
nPnD (True negative?)

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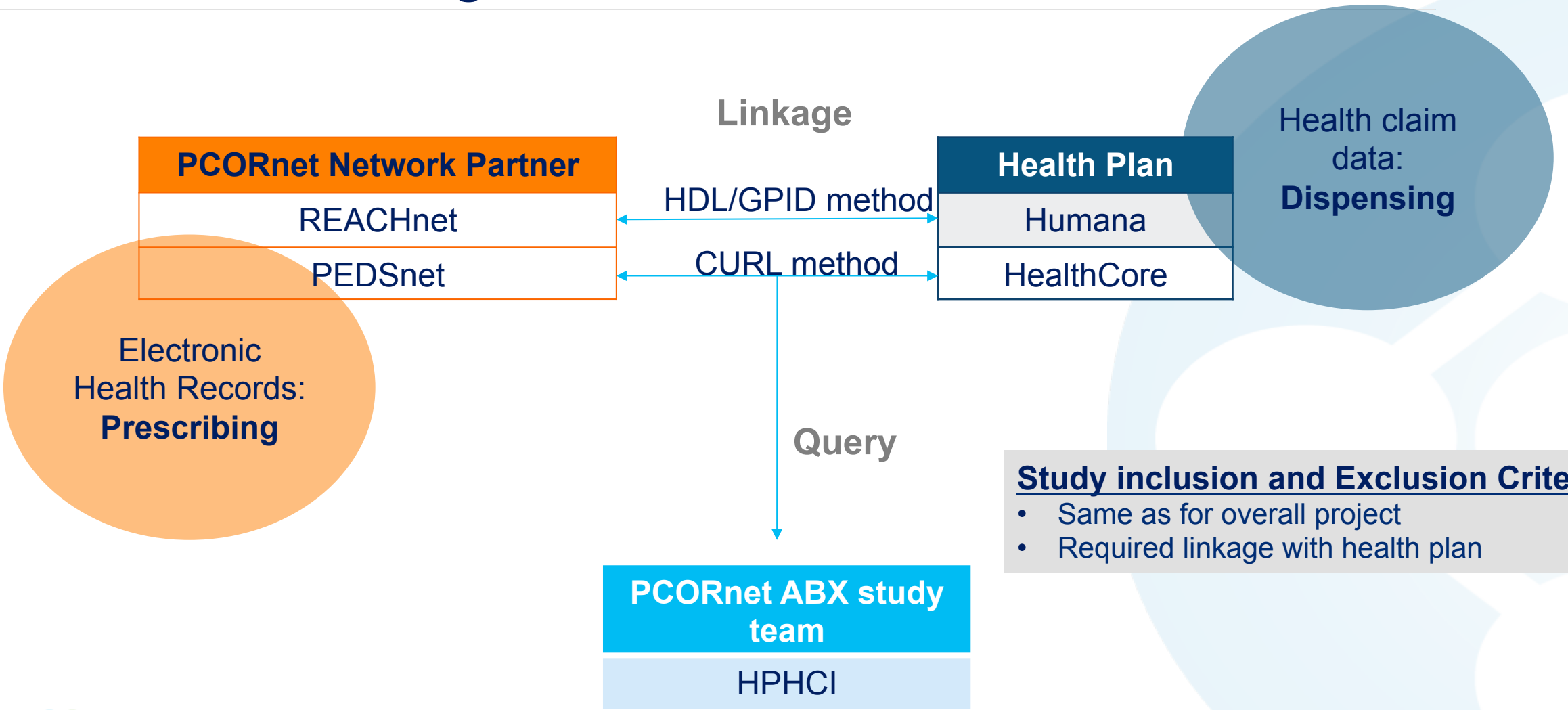
Health-Plan Linkage



Study inclusion and Exclusion Criteria

- Same as for overall project
- Required linkage with health plan

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Demographics of ABX study and HP-linked populations

	Main ABX Study	PEDSnet	PEDSnet/ HealthCore Linkage	REACHnet	REACHnet/ Humana Linkage
Total Patients	681,739	317,435	4,792	8,451	549
Sex					
.Male	52%	53%	58%	53%	54%
.Female	48%	47%	42%	47%	46%
Race					
.White	53%	48%	76%	63%	80%
.Black/Afr Am	25%	32%	9%	32%	17%
.Asian	4%	3%	3%	3%	2%
.Other/unk	18%	17%	11%	2%	1%

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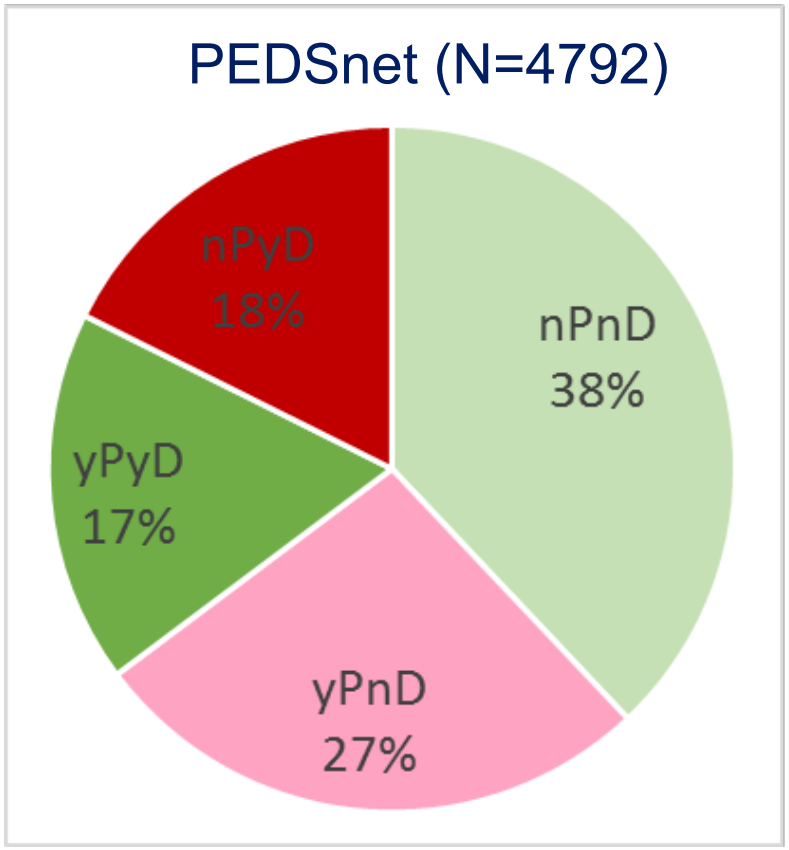
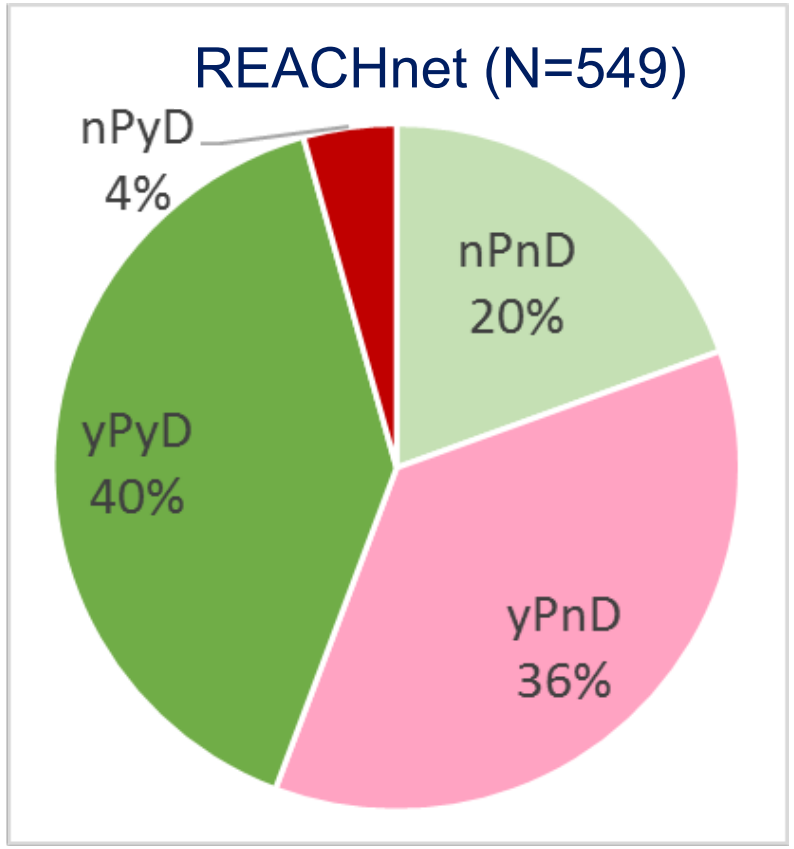
Presence of prescription & dispensing between age 0 to <2 years





- No prescription no dispensing (nPnD)
- Prescription but no dispensing (yPnD)
- Both prescription and dispensing (yPyD)
- No prescription but Dispensing (nPyD)

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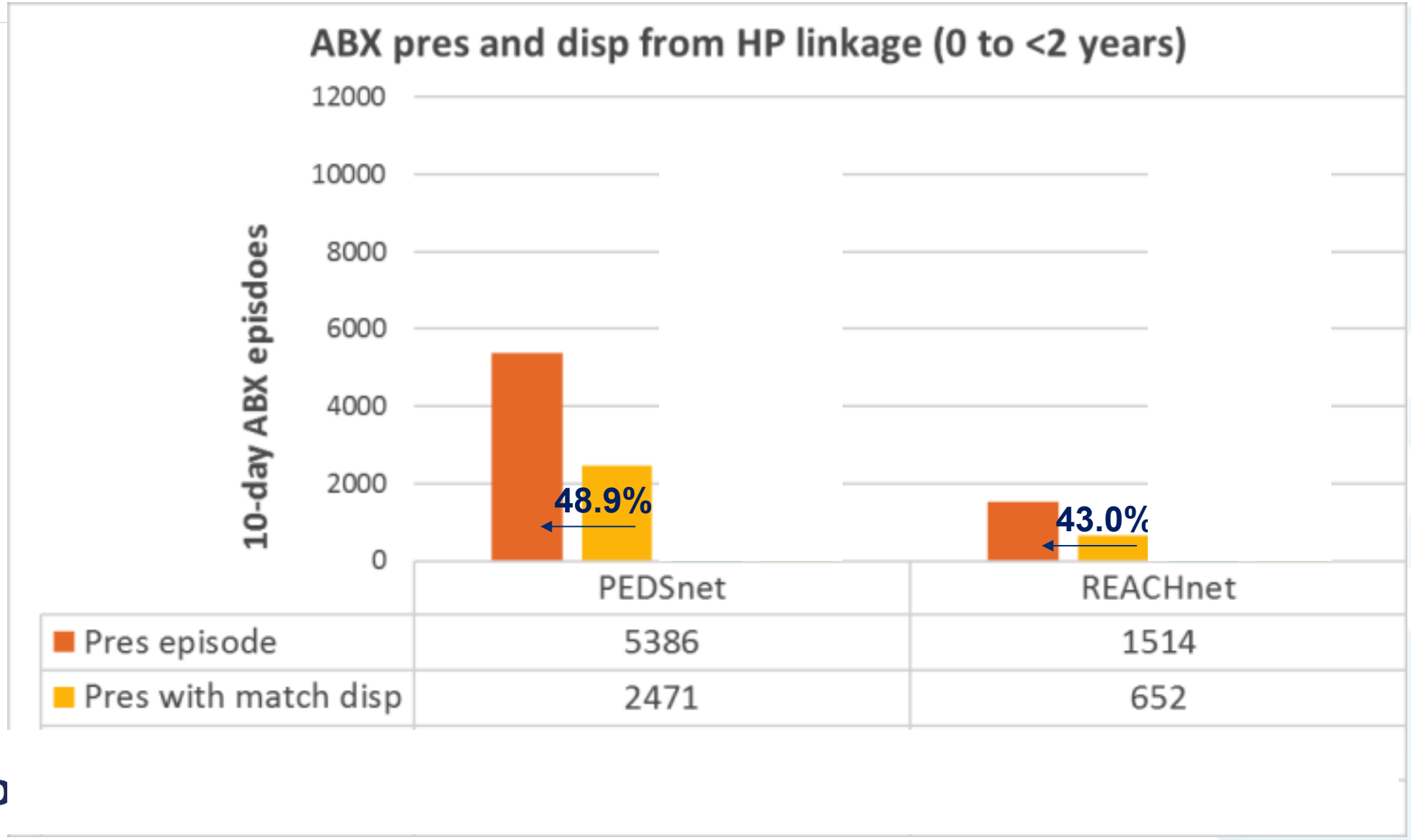
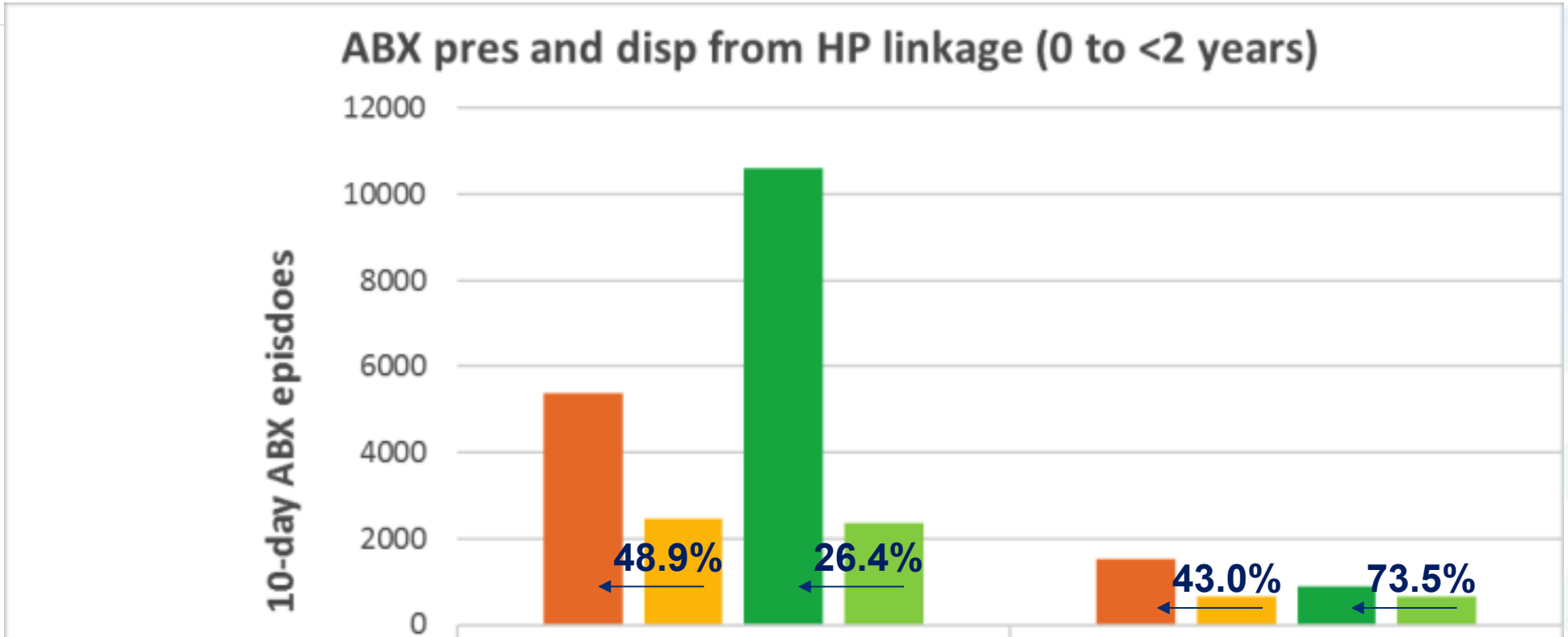
Matching between prescribing and dispensing episodes



Matching between prescribing and dispensing episodes



	PEDSnet	REACHnet
Pres episode	5386	1514
Pres with match disp	2471	652
Disp episode	10611	889
Disp with match pres	2371	653

Discussion

- As common in other health care systems prescriptions may be written across multiple institutions or organizations
- Prescription dispensings may have varying degrees of completeness within administrative data systems
- Data linkage can close gaps between prescriptions written and prescription dispensings
- PCORnet is closing gaps in data to support patient-centered real world evidence development

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U.S. FOOD & DRUG ADMINISTRATION

Heterogeneity as a Source of Strength: The Value of International and Prescribing Data to FDA

Michael D. Nguyen, MD
Sentinel Program Lead
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research
August 26, 2019

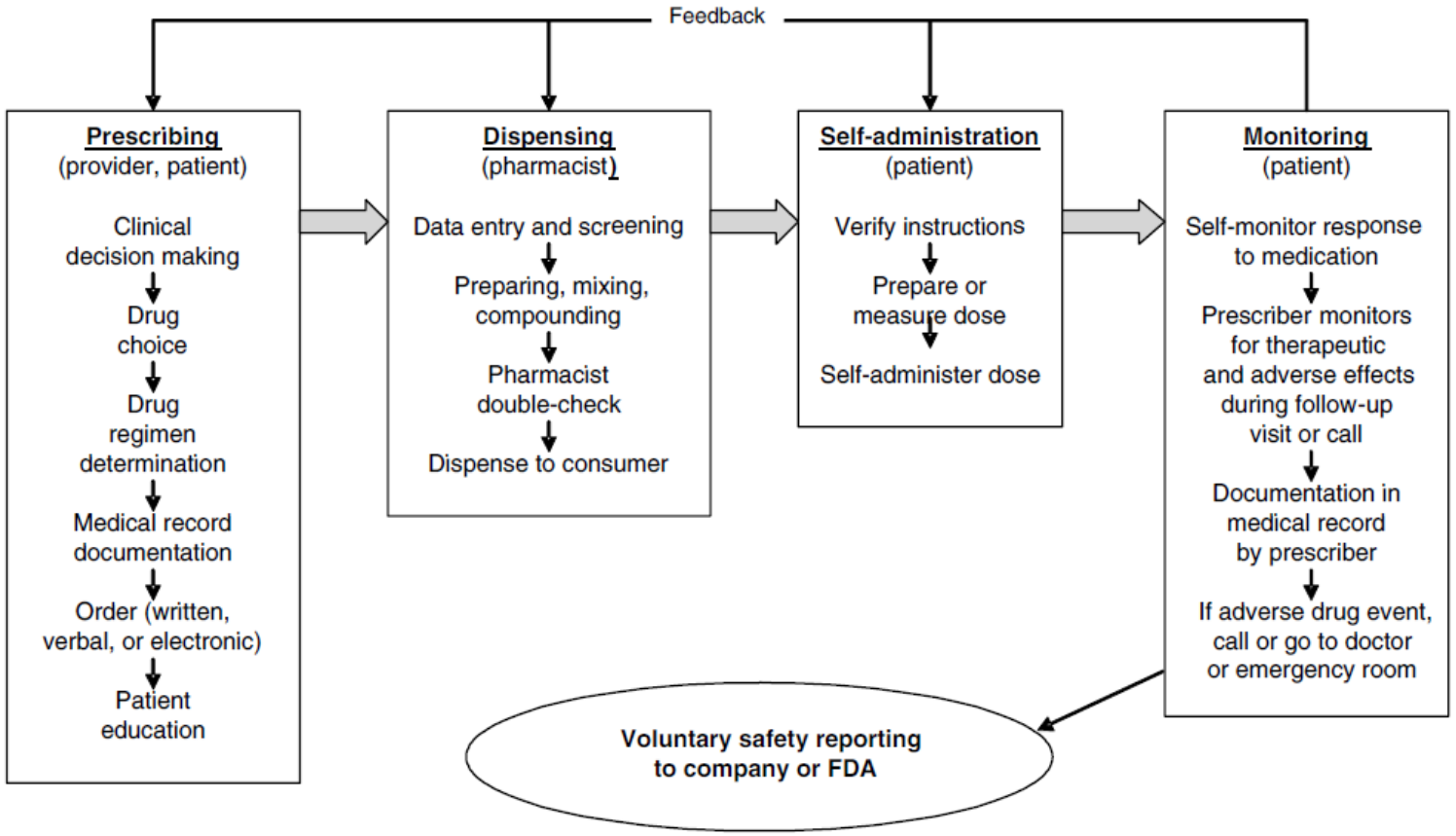
Symposium Themes Thus Far

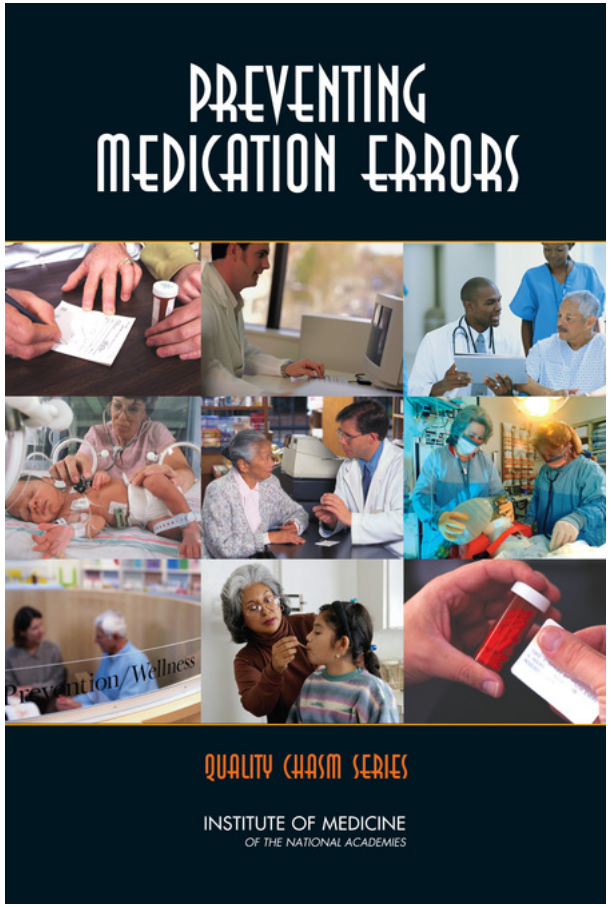
- FDA's international collaboration efforts demonstrate the flexibility of multi-site distributed data networks to incorporate a variety of data sources and reach across national borders
  - Shows extensibility and flexibility of Sentinel's common data model and analysis tools
  - Exemplifies how all participants can benefit from shared infrastructure
- Two new dimensions: prescribing data and country-specific data
  - Illustrates how heterogeneity of data sources can be a source of strength and improve our understanding of medication utilization when used appropriately
  - Defining exposed time should account for the differences between prescribing and dispensing data streams, as well as other country-specific factors

Outline

- What different types of regulatory questions might be addressed with prescribing data?
  - Prescribing data alone
  - Prescribing data in combination with dispensing data
- How international drug utilization data might help regulatory agencies

Medication Use Process in Community Care





https://www.nap.edu/catalog/11623/preventing-medication-errors

Potential Regulatory Questions to Pursue

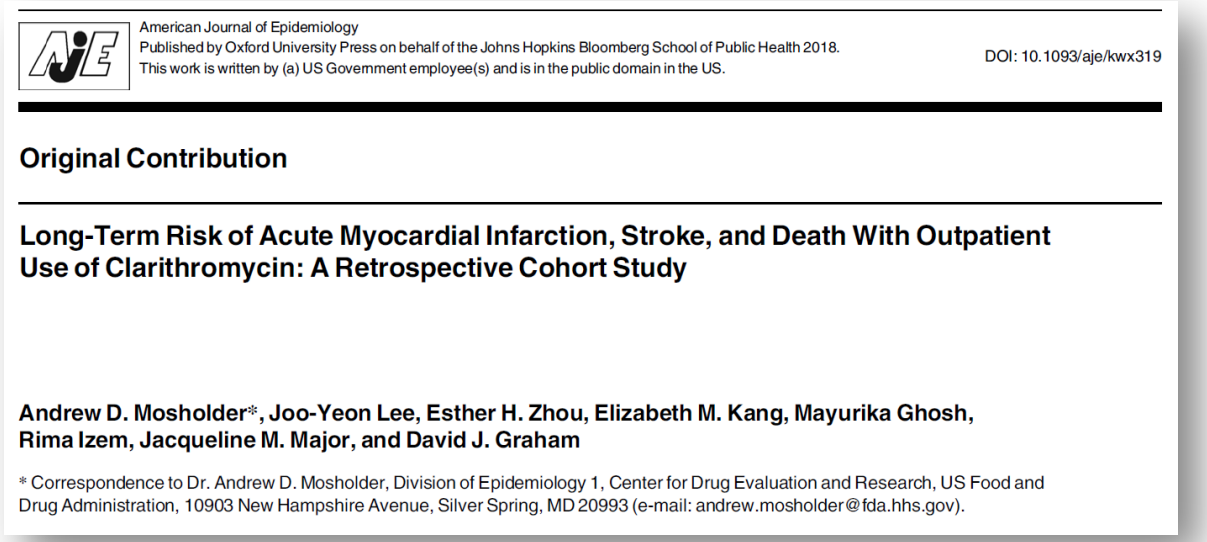
Prescribing Data Alone

- Drug utilization (e.g., use in pregnancy)
- Inferential safety studies
- Rates of proprietary name use
- Impact of proprietary name change interventions

Prescribing Linked to Dispensing Data

- Medication errors
  - Wrong drug, dose, frequency
  - Name confusion
- Prescribing vs. dispensing substitutions or change rates
- Assess rates of “dispensed as written” prescriptions as potential indicator of concerns about therapeutic inequivalence

FDA Studies Using CPRD Prescribing Data



American Journal of Epidemiology
Published by Oxford University Press on behalf of the Johns Hopkins Bloomberg School of Public Health 2018.
This work is written by (a) US Government employee(s) and is in the public domain in the US.

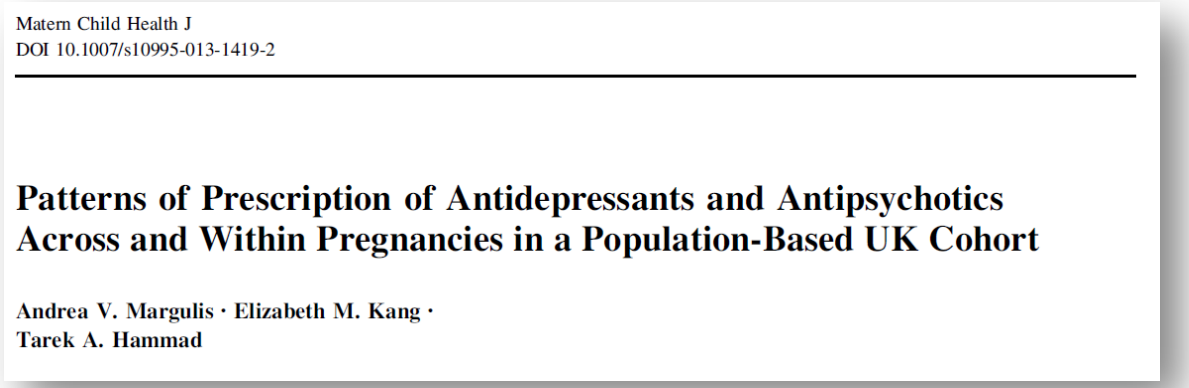
DOI: 10.1093/aje/kwx319

Original Contribution

Long-Term Risk of Acute Myocardial Infarction, Stroke, and Death With Outpatient Use of Clarithromycin: A Retrospective Cohort Study

Andrew D. Mosholder*, Joo-Yeon Lee, Esther H. Zhou, Elizabeth M. Kang, Mayurika Ghosh, Rima Izem, Jacqueline M. Major, and David J. Graham

* Correspondence to Dr. Andrew D. Mosholder, Division of Epidemiology 1, Center for Drug Evaluation and Research, US Food and Drug Administration, 10903 New Hampshire Avenue, Silver Spring, MD 20993 (e-mail: andrew.mosholder@fda.hhs.gov).



Matern Child Health J
DOI 10.1007/s10995-013-1419-2

Patterns of Prescription of Antidepressants and Antipsychotics Across and Within Pregnancies in a Population-Based UK Cohort

Andrea V. Margulis · Elizabeth M. Kang · Tarek A. Hammad

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2013)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3462

ORIGINAL REPORT

Use of selective serotonin reuptake inhibitors in pregnancy and cardiac malformations: a propensity-score matched cohort in CPRD†

Andrea V. Margulis, Adel Abou-Ali, Marian M. Strazzeri, Yulan Ding, Fatmatta Kuyateh, Eric Y. Frimpong, Mark S. Levenson and Tarek A. Hammad*

PHARMACOEPIDEMIOLOGY AND DRUG SAFETY (2013)
Published online in Wiley Online Library (wileyonlinelibrary.com) **DOI**: 10.1002/pds.3549

ORIGINAL REPORT

Risk of acute myocardial infarction, stroke, or death in patients initiating olmesartan or other angiotensin receptor blockers — a cohort study using the Clinical Practice Research Datalink†

Esther H. Zhou[1,*,‡], Kate Gelperin[1‡], Mark S. Levenson[2], Martin Rose[3], Ya-Hui Hsueh[2] and David J. Graham[1]

[1] *Office of Surveillance and Epidemiology, U.S. Food and Drug Administration, MD, USA*
[2] *Office of Biostatistics, U.S. Food and Drug Administration, MD, USA*
[3] *Office of New Drugs, U.S. Food and Drug Administration, MD, USA*

Institute for Safe Medication Practices

High-Alert Medications in Ambulatory Settings

Classes/Categories of Medications	Specific Medications
antiretroviral agents (e.g., efavirenz, lami**VUD**ine, raltegravir, ritonavir, combination antiretroviral products)	car**BAM**azepine
chemotherapeutic agents, oral (excluding hormonal agents) (e.g., cyclophosphamide, mercaptopurine, temozolomide)	chloral hydrate liquid, for sedation of children
hypoglycemic agents, oral	heparin, including unfractionated and low molecular weight heparin
immunosuppressant agents (e.g., aza**THIO**prine, cyclo**SPORINE**, tacrolimus)	met**FORMIN**
insulin, all formulations	methotrexate, non-oncologic use
opioids, all formulations	midazolam liquid, for sedation of children
pediatric liquid medications that require measurement	propylthiouracil
pregnancy category X drugs (e.g., bosentan, **ISO**tretinoin)	warfarin

https://www.ismp.org/recommendations/high-alert-medications-community-ambulatory-list

Received: 31 December 2018 | Revised: 7 May 2019 | Accepted: 12 June 2019

DOI: 10.1002/pds.4858

ORIGINAL REPORT

WILEY

Development of an algorithm to detect methotrexate wrong frequency error using computerized health care data

Lisa J. Herrinton[1] | Tiffany S. Woodworth[2] | Efe Eworuke[3] | Laura B. Amsden[1] | Liyan Liu[1] | Jo Wyeth[3] | Andrew Petrone[2] | Talia J. Menzin[2] | James Williams[2] | Robert Goldfien[1] | Michael Nguyen[3]

Having access to the prescribing and dispensing data allowed FDA to assess and control for the potential contribution of prescribing behaviors

https://onlinelibrary.wiley.com/doi/epdf/10.1002/pds.4858

RECOMMENDATIONS

List of Confused Drug Names

February 28, 2019

ISMP's List of Confused Drug Names contains look-alike and sound-alike (LASA) name pairs, of medications that have been published in the *ISMP Medication Safety Alert!®* and the *ISMP Medication Safety Alert!® Community/Ambulatory Care* Edition through February 28, 2019.

Use this list to determine which medications require special safeguards to reduce the risk of errors and minimize harm. This may include strategies such as:

*ce**FAZ**olin*	*cef**TRIAX**one*
*cef**TRIAX**one*	*ce**FAZ**olin*
cefuroxime	*sulfa**SALA**zine*
Cele**BREX**	Cele**XA**
Cele**BREX**	Cerebyx
Cele**XA**	Cele**BREX**
Cele**XA**	Cerebyx
Cele**XA**	Zy**PREXA**
Cerebyx	Cele**BREX**
Cerebyx	Cele**XA**
cetirizine	*sertraline*

https://www.ismp.org/recommendations/confused-drug-names-list

Value of International Collaboration

- Different drug approval dates allow regulators to leverage postmarket safety information from other countries for more timely safety data
- Different uptake patterns and underlying populations (race, ethnicity, BMI, smoking, etc.) allow subgroup analyses
- Differences in healthcare systems may impact duration of medication adherence or duration of observation creating new opportunities
- Pooling of smaller populations may lead to more precise population level risk estimates (e.g., pregnancy, pediatrics, rare diseases, orphan drugs)

Adherence to Drugs May Differ

Cost-Related Prescription Nonadherence in the United States and Canada: A System-Level Comparison Using the 2007 International He

Jae Kennedy, PhD[1]; anc

[1]Department of Health Poli
Spokane, Washington; and
and Public Health, Universi

ABSTRACT

Background: Prior researc
of the United States are near
nadian residents to report c
(CRNA) (ie, being unable to f
cost). However, these kinds
obscure important within-c
surance coverage.

Table II. Odds ratios for cost-related nonadherence (CRNA)* among working-age adults (<65 years of age) in Canada and the United States, by insurance system.

Insurance System	N (1000s)	CRNA, %	Adjusted Odds Ratio (95% CI)†
Canadian compulsory coverage (Quebec)	242	4.4	**0.5 (0.3–0.8)**
Canadian senior and social assistance coverage (Ontario)	727	8.8	Reference
Canadian income-based coverage (British Columbia, Manitoba, and Saskatchewan)	487	12.1	1.4 (1.0–2.1)
Canadian mixed coverage (all other provinces)	431	11.0	1.3 (0.9–1.9)
US private coverage (employer-based or individual)	14,810	15.9	**2.2 (1.6–3.0)**
US senior and social assistance coverage (Medicare, Medicaid, or other)	7447	22.2	**2.2 (1.4–3.5)**
US no coverage (uninsured during past year)	25,755	43.3	**7.2 (5.0–10.5)**

*Defined as inability to pay for a prescribed medication.
†Adjusted model controls for gender, income, and chronic illness; significant odds ratios in boldface.
Source: 2007 International Health Policy Survey in Seven Countries.[32]

International Product Quality Issue

FDA U.S. FOOD & DRUG ADMINISTRATION

Search Menu

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

26 April 2019
EMA/241020/2019

Update on nitrosamine impurities: EMA continu to prevent impurities in medicines

Following an EU safety review, which concluded on strict legally binding limits for nitrosamine impurities in sartan blood pressure medicines, EMA continues to work to ensure manufacturers are taking appropriate measures to avoid or keep impurities below acceptable limits.

Based on experience from the review of sartans, EMA is launching an exercise with experts from across the EU regulatory network including national authorities, the European Directorate for the Quality of Medicines & HealthCare (EDQM) and the European Commission to consider how to prevent such incidents in future and to see if their management can be improved, should they occur.

EMA will publish the outcome of the exercise in due course, including information on any further actions that may be required.

MHRA has recalled 3 batches of Losartan tablets due to contamination with the nitrosamine N-nitroso-N-methylamino butyric acid.

Published 21 March 2019
From: Medicines and Healthcare products Regulatory Agency

ing detection of an impurity

veet Linkedin

Government of Canada | Gouvernement du Canada | Canada.gc.ca | Services | Departments | Français

Recalls and safety alerts — Canada

Recalls & alerts | Kids | Food | Your Health | Environment | Consumer products

Home » Recalls & alerts — Share | Contrast | Print

Multiple Losartan-containing drugs voluntarily recalled because of potential for nitrosamine impurity

Starting date:	March 9, 2019
Type of communication:	Information Update
Subcategory:	Drugs
Source of recall:	Health Canada
Issue:	Important Safety Information
Audience:	General Public
Identification number:	RA-69272

Report a Concern

- What you should do
- Media enquiries
- Public enquiries

March 9, 2019
For immediate release

Potential International Analysis in Sentinel

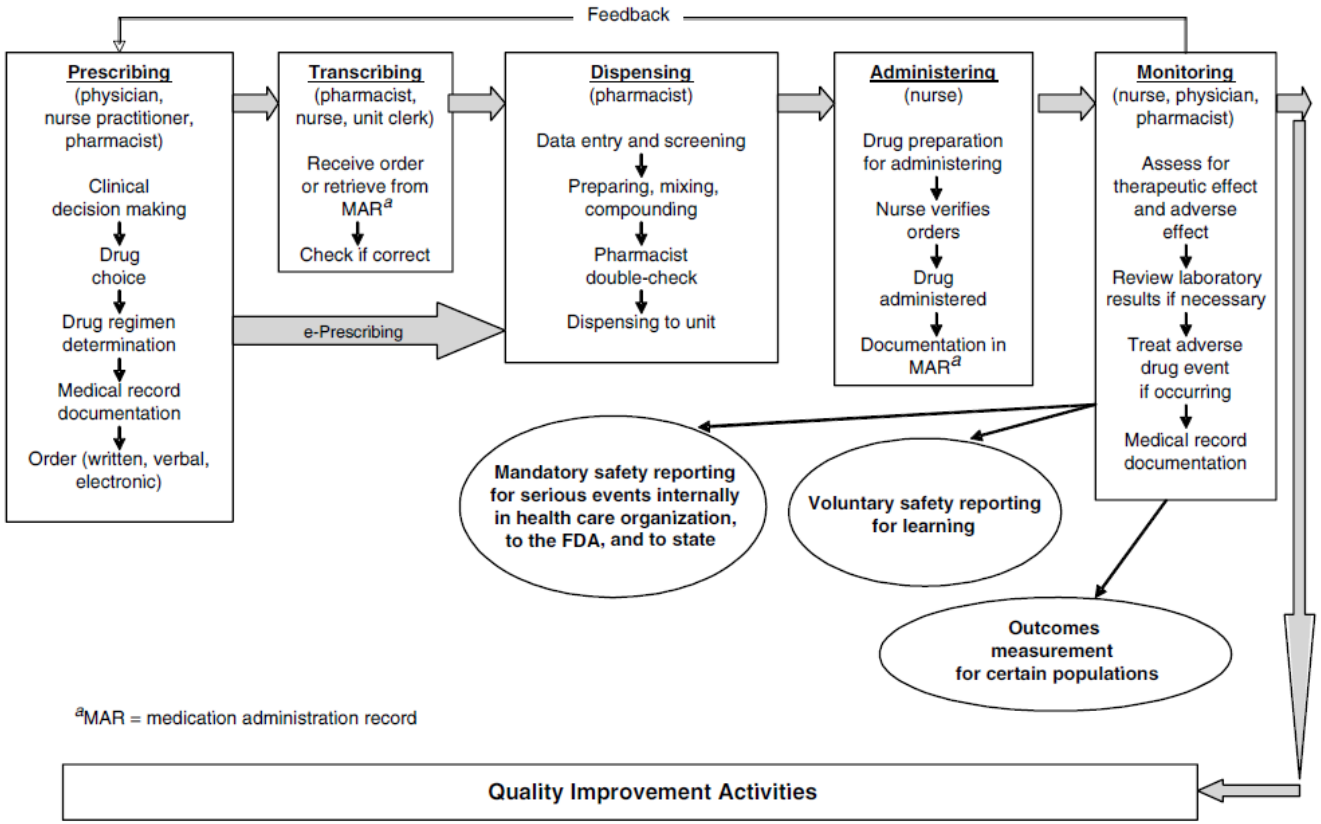
- In July 2018, international regulatory agencies ordered the recall of angiotensin receptor blockers.
- Public communications emphasized that patients should not stop their medication. It is unknown how these safety communications affected prescribing behavior and use.
- Assess impact of drug safety communications and recalls in USA, Canada, UK and other countries.
- Develop a single, common analytic package using data formatted in the Sentinel CDM.
- Assess drug switching to non-recalled products or alternative drugs, and drug discontinuation trends, possibly using interrupted time series analysis.
- Assess differential impact of public health interventions between countries to inform future global health responses.

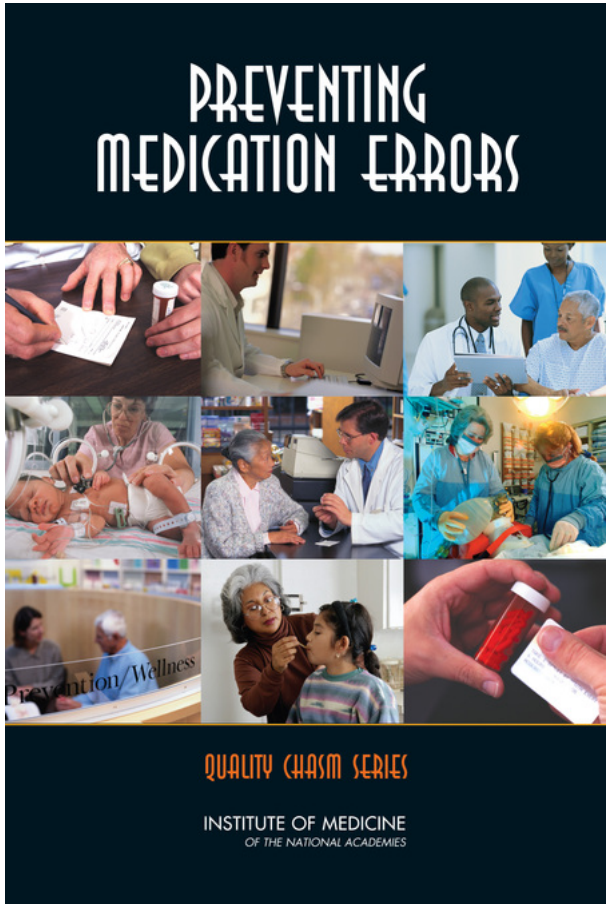
Summary

- The expanded Sentinel CDM that integrates prescribing data, coupled with international data harmonization efforts in CNODES and UK has created new opportunities to improve public health.
- The single common analytic platform allows countries to evaluate global public health issues in a unified approach
  - Leverages the relative strengths and unique features of each country
  - Offers the ability for combined analysis for more robust descriptive or inferential analyses
- FDA will continue to explore ways to encourage international collaboration using the Sentinel CDM and analytic tools


FDA
U.S. FOOD & DRUG
ADMINISTRATION

Medication Use Process in Hospital and Long Term Care





https://www.nap.edu/catalog/11623/preventing-medication-errors