Adverse drug event presentations to outpatient medications: an analysis of hospital presentations

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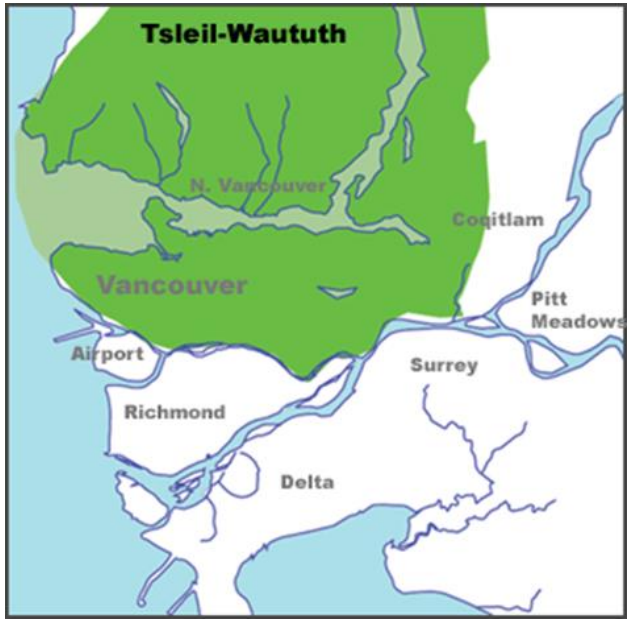
We would like to acknowledge that we are gathered today on the traditional territories of the Musqueam, Squamish and Tsleil-Waututh peoples.

Source: www.johomaps.net/na/canada/bc/vancouver/firstnations/firstnations.html



Acknowledgements

ActionADE was developed by UBC (Hohl) and SFU (Balka) researchers in partnership with patient partners, clinicians, VCH, MoH, and Excellar Technologies with financial and in-kind contributions from CIHR, VGH, MoH, CPBC and Health Research BC organizations.

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Objectives

- Review adverse drug event presentations to outpatient medications in emergency departments
- Describe system-level issues that lead to repeat adverse drug events
- Gain an understanding of how technology might help us break down silos in care and keep patients safe
- Present research methods to help understand whether health equity stratifiers are associated with adverse drug event reporting.

Glen's Story

Why we report

Watch Glen's Story

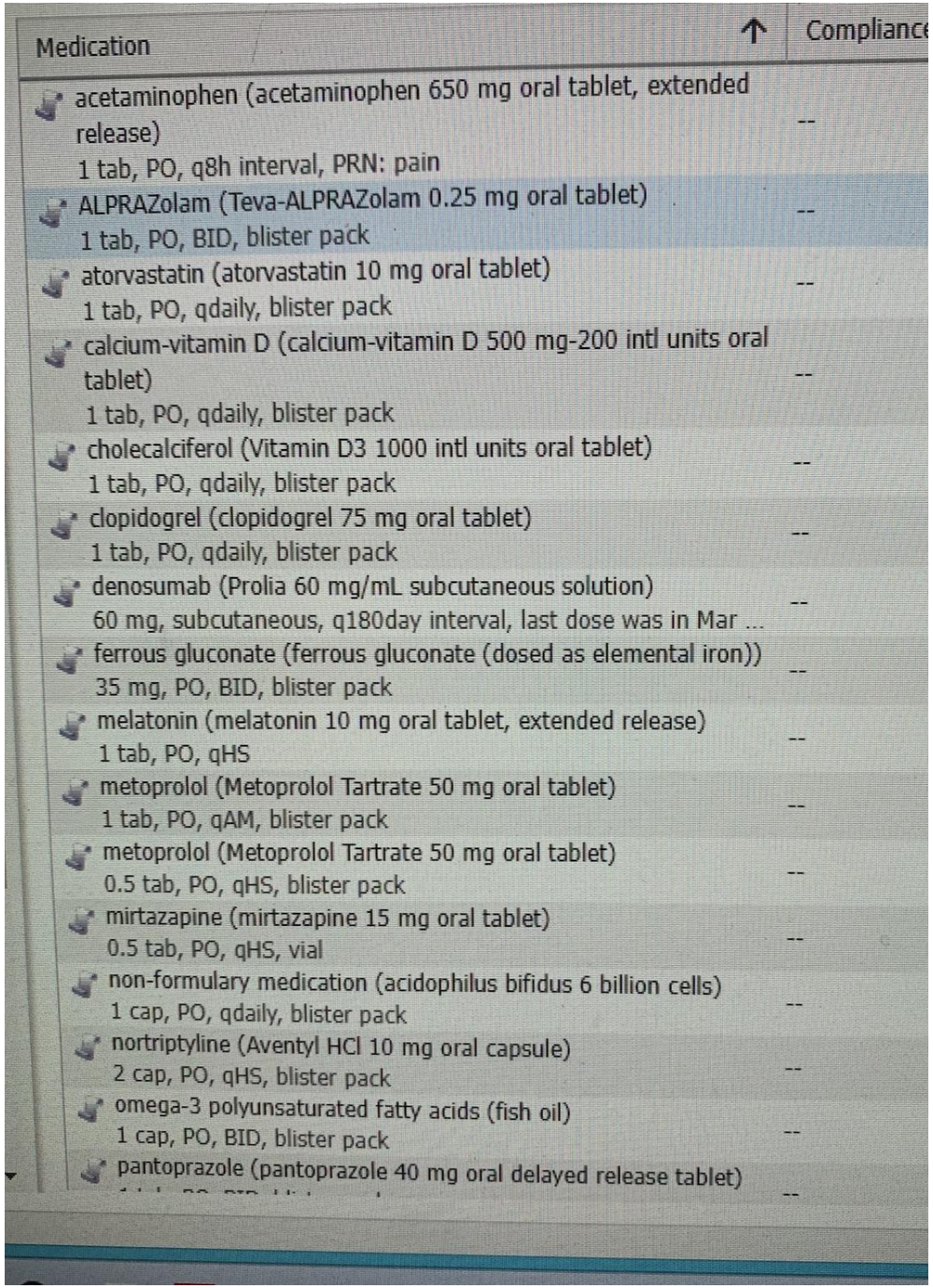
From my last shifts

Case from Sept 28, 2025

- 78F independent presents from home with a fall
- Took medications at 2330 and woke up at 0330 to urinate, felt dizzy (not vertiginous) and groggy and lost her balance
- No obvious medical cause for falls, and not UTI symptoms
- ED work-up for a medical cause for the fall: negative
- ED work-up for traumatic complications: negative

Falls in older people are associated with loss of quality of life, autonomy, and increased risk of institutionalization and death

Case from Sept 28, 2025



Medication	Compliance
acetaminophen (acetaminophen 650 mg oral tablet, extended release) 1 tab, PO, q8h interval, PRN: pain	--
ALPRAZolam (Teva-ALPRAZolam 0.25 mg oral tablet) 1 tab, PO, BID, blister pack	--
atorvastatin (atorvastatin 10 mg oral tablet) 1 tab, PO, qdaily, blister pack	--
calcium-vitamin D (calcium-vitamin D 500 mg-200 intl units oral tablet) 1 tab, PO, qdaily, blister pack	--
cholecalciferol (Vitamin D3 1000 intl units oral tablet) 1 tab, PO, qdaily, blister pack	--
clopidogrel (clopidogrel 75 mg oral tablet) 1 tab, PO, qdaily, blister pack	--
denosumab (Prolia 60 mg/mL subcutaneous solution) 60 mg, subcutaneous, q180day interval, last dose was in Mar ...	--
ferrous gluconate (ferrous gluconate (dosed as elemental iron)) 35 mg, PO, BID, blister pack	--
melatonin (melatonin 10 mg oral tablet, extended release) 1 tab, PO, qHS	--
metoprolol (Metoprolol Tartrate 50 mg oral tablet) 1 tab, PO, qAM, blister pack	--
metoprolol (Metoprolol Tartrate 50 mg oral tablet) 0.5 tab, PO, qHS, blister pack	--
mirtazapine (mirtazapine 15 mg oral tablet) 0.5 tab, PO, qHS, vial	--
non-formulary medication (acidophilus bifidus 6 billion cells) 1 cap, PO, qdaily, blister pack	--
nortriptyline (Aventyl HCl 10 mg oral capsule) 2 cap, PO, qHS, blister pack	--
omega-3 polyunsaturated fatty acids (fish oil) 1 cap, PO, BID, blister pack	--
pantoprazole (pantoprazole 40 mg oral delayed release tablet)	--

Case from Sept 28, 2025

- She had taken *blister-packed* evening doses of
  - Alprazolam 0.25mg po → sedation
  - Melatonin 10mg po → sedation, dizziness
  - Mirtazapine 7.5mg po → imbalance, dizziness, sedation, falls
  - Nortriptyline 20mg po → imbalance, dizziness, sedation, falls

Case from either Sept 29 or Oct 6, 2025

- 76F independent presents from home with her husband after successful MVR for mitral regurgitation. Discharged on Amiodarone and Bisoprolol for atrial fibrillation
- 4 days ago, husband thought she was experiencing medication toxicity with increasing nausea and vomiting, and bradycardia with heart rate in the 40's
- Husband woke up to her trying to get out of bed. She was unable to get up and collapsed back into bed in cardiac arrest
- Immediate CPR and 911 activation:
  - EHS arrived – no shock advised → Epinephrine → ROSC

On two beta-blocking agents, with Bisoprolol renally metabolized and low GFR. No alternate cause identified in CCU. Discharged home.

Adverse Drug Events

Dr. Corinne Hohl

Adverse Drug Events

Prospective Canadian Studies

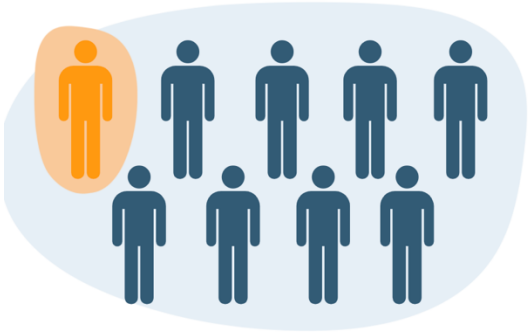
Period of Data Collection	Sites	Sample Size	ADE frequency, % (95% CI)
2008	1	1017	12.0 (10.1-14.2)
2012	2	1591	8.2 (7.0-9.7%)
2018	3	1529	12.0 (10.4-13.8%)

Our studies indicate that emergency physicians miss or are uncertain about the ADE diagnosis in 40-50% of cases.

Zed et al., Incidence, severity and preventability of medication-related visits to the ED: a prospective study. CMAJ 2008.
Hohl et al., Clinical Decision Rules to Improve the Detection of Adverse Drug Events in Emergency Department Patients. Acad Emerg Med 2012.
Hohl et al., Prospective Criteria to Identify ED Patients at High-Risk of Adverse Drug Events in the ED. Acad Emeg Med 2018.
Hohl et al. Do Emergency Physician Recognition of Adverse Drug-Related Events in Elder Patients Presenting to an Emergency Department? Acad Emerg Med 2005.
Hohl et al. Do Emergency Physician Attribute Drug-Related ED Visits to Medication-Related Problems? Ann of Emer Med 2010.

ADE Incidence

- Outpatient medications cause or contribute to 8-12% of ED Visits



- This approximates to:
  - 279,000 ED visits across BC each year
  - 103,000 hospital admissions across BC each year
  - Costs upwards of $2 billion annually

Hohl CM et al. Ann Emerg Med 2001; 38(6): 666-71.
Hohl CM et al. Acad Emerg Med 2012; 19(6):640-9.
Hohl CM et al. CMAJ Open 2019; 7(3): 446-53.
Zed PJ et al. CMAJ 2008; 178 (12): 1563-9.

Pharmacists observed the following phenomenon over and over again

“I saw a diabetic today who was discharged from MSJ, where he presented comatose because of low blood sugar due to glyburide. The physician there asked him to stop the glyburide, and gave him a prescription for gliclazide, an agent with a lower risk of causing hypoglycemia. The patient presented to VGH a few days later with a critically low blood sugar, was treated, and then became hypoglycemic again. When I looked at the patient's blister pack I was horrified to discover both glyburide and gliclazide had been dispensed. It turns out the patient had been given a discharge prescription for gliclazide, and had been told to discontinue the glyburide. Neither the GP nor the community pharmacist were aware of what had happened, and the patient didn’t understand the instructions.”

VGH pharmacist

What proportion of adverse drug events are repeat events?

Repeat ADE's

1 in 3

ADEs were repeat ADE's

3 in 4

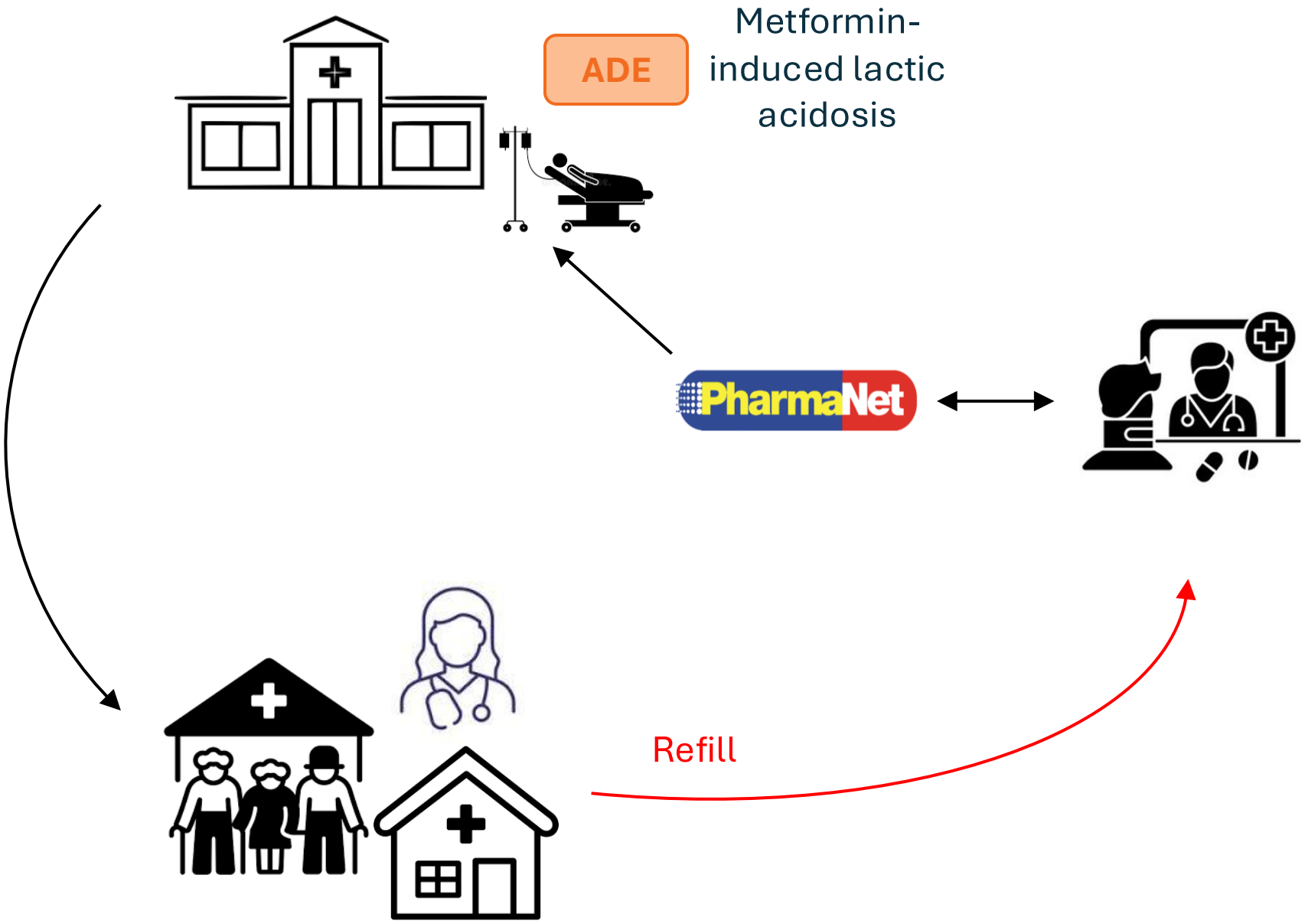
repeat ADEs were probably or definitely preventable

- Unstandardized documentation and suboptimal communication of adverse drug events were identified as major contributing factors

Hohl CM et al. CMAJ Open 2019; 7(3): 446-53.

Why?

Why?



Glen's Story

In **Cerner Discharge Summaries** from 2020 and 2021:

Stop Taking the Following Home Medications

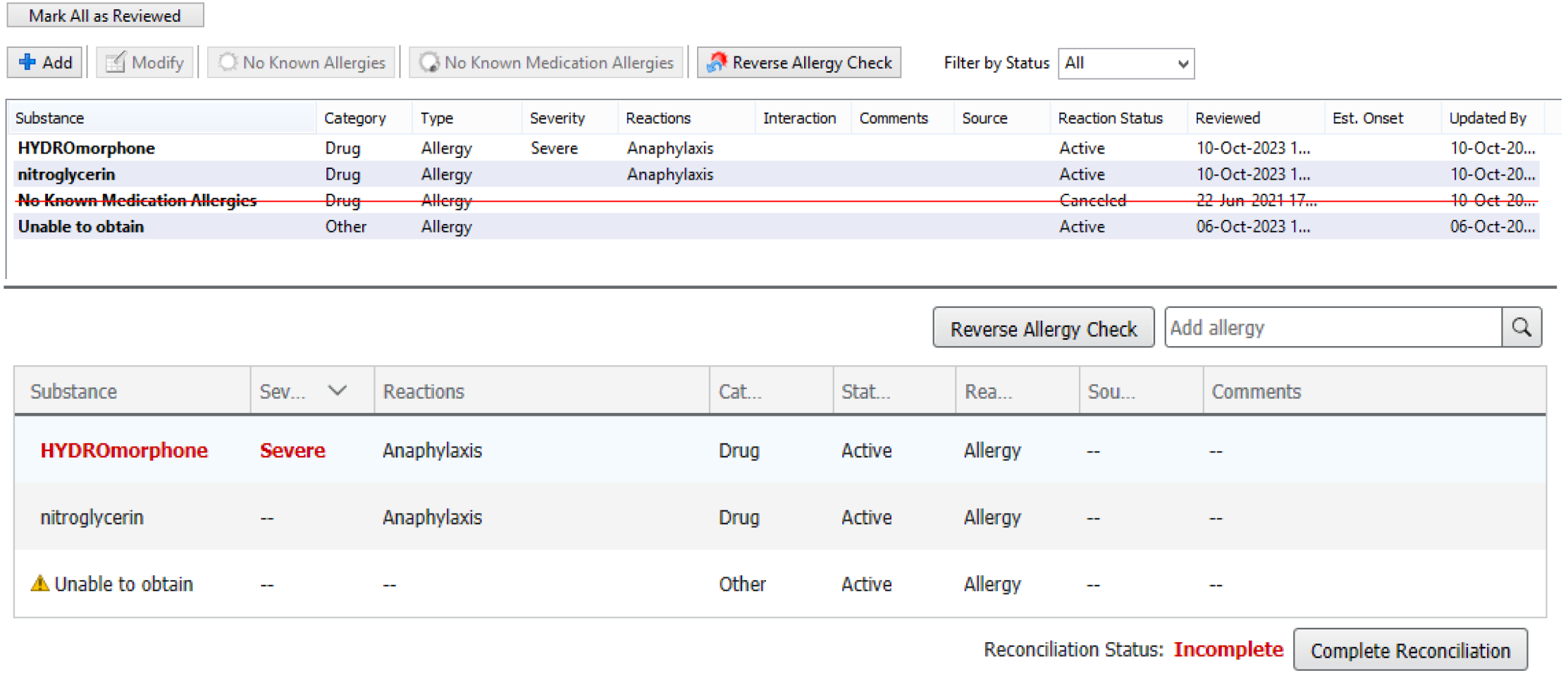
Medication	Reason to Stop Taking
empagliflozin	
metFORMIN	
ramipril	

Stop Taking the Following Home Medications

Medication	Reason to Stop Taking
empagliflozin (Jardiance 25 mg oral tablet)	
gliCLAZide (gliclazide 30 mg oral tablet, extended release)	
metFORMIN (metFORMIN 500 mg oral tablet)	

Glen's Story

In **Cerner Allergy Form** after his discharge:



An Introduction to ActionADE

Dr. Corinne Hohl

Creating Interoperability

What is ActionADE?

ActionADE is a web-based application that allows providers to document and communicate standardized **adverse drug event (ADE)** information to providers in other health settings to **prevent unintentional re-exposures** to harmful medications.

🎯 Our Goal

To document and communicate ADE information in a way that is universally understood by care providers.

To share ADE information with pharmacists and physicians in a platform that follows patients across health sectors to alert other providers.

Systematic Reviews on Underreporting

- Reviewed 37 studies, regardless of methods: “median underreporting 94%”
- Weighted mean proportion of underreporting >97%.

Moride et al.[22]	France	81 GPs monitoring for 3 days	All	1	24 433	>99
			Serious	1	6123	>99
Montastruc et al.[23]	France	3 GPs monitoring for 3 months	All	1	2937	>99
Fletcher[24]	UK	Adverse event data from PMS (7 drugs)	All	202	12 093	98
Lumley et al.[25]	UK	24 GP practices monitoring for 4 weeks	All	35	576	94
			Severe	2	10	80

Are the spontaneously reported data representative?

Focus groups with practicing Clinicians

FACTORS CONTRIBUTING TO UNDERREPORTING

REPORTING FORM DESIGN

- **Length:** Average ~35 data fields
- **Nature of information collected:** Forms designed to meet research / regulation needs vs. clinical care
- **Separate access:** Provider must fill out paper form or access website external to EMR
- **Duplicate data entry:** Providers must re-enter data previously input into clinical EMR
- **Inflexible data entry:** Difficult or impossible to input and explain complex events appropriately or enter events in process

CLINICIAN BELIEFS, PRIORITIES & PRACTICES

- **Patient care > Data needs:** Providers choose to focus on immediate patient needs
- **Familiarity with reporting programs or practices:** Providers unfamiliar with where and what to report
- **Perceived ineffectiveness of reporting programs:** Skepticism about utility and relevance of reporting
- **Other methods of communicating around ADRs:** Clinicians use informal methods to address ADRs (e.g. contact other providers by fax/phone, advise patient)

UNCERTAIN NATURE OF ADVERSE DRUG REACTIONS

- **Fuzziness of ADR definitions:** Varying interpretations of what constitutes an ADR
- **Difficulty diagnosing ADRs and establishing causality:** ADRs appear in patients with complex medication regimens, combined with known and unknown underlying conditions
- **Complex / unique situations:** Many ADEs involve multiple interacting factors (e.g. adherence, provider decisions/mistakes, changing medication regimens)
- **Time required for ADRs to unfold:** Rare for a single provider to observe the entire course of a single ADR

Serious ADR reporting mandated in 2019

- To improve increase the quantity and quality of serious ADR and medical device incident reports received by Health Canada to increase their ability to identify safety signals earlier.
- To detect safety events that cannot be uncovered in randomized trials (real-life use, off-label use, rare, etc.)

Vanessa Young

Vanessa's Law

- Amendments to the *Food and Drugs Act* include:

1. Power to require information, tests or studies
2. Power to require a label change/package modification
3. Power to recall unsafe therapeutic products
4. Ability to disclose information in certain circumstances
5. Tougher measures for those that do not comply
6. **Mandatory reporting of serious adverse drug reactions and medical device incidents by health care institutions**

Vanessa's Law allows Health Canada to:

- Require information, tests, or studies
- Recall unsafe therapeutic products
- Require label changes and package modifications
- Require mandatory reporting by hospitals of serious adverse drug reactions (ADRs) and medical device incidents (MDIs)

The law has clout and specifies imprisonment for up to 2 years and fines up to $5,000,000 if contravened.

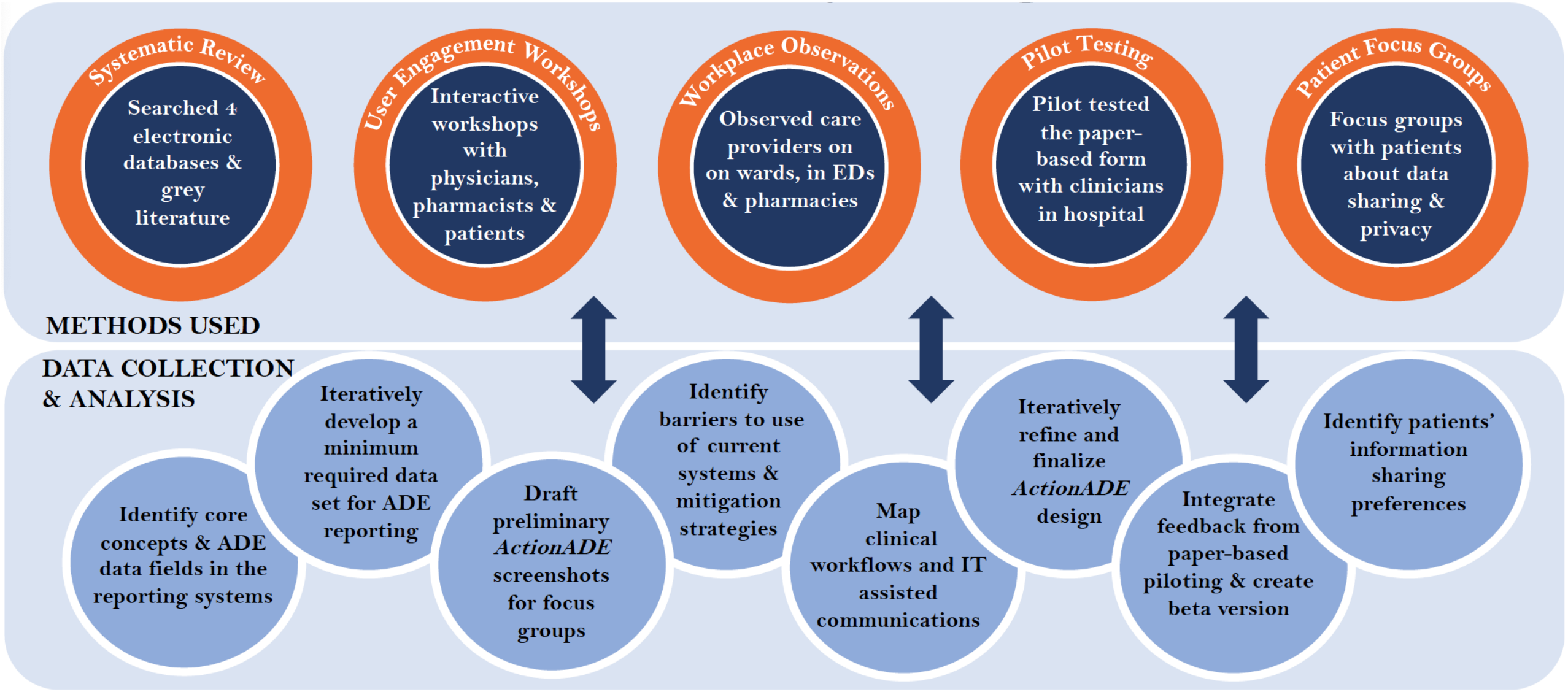
Why was ADR reporting made mandatory?

- To improve increase the quantity and quality of serious ADR and medical device incident reports received by Health Canada to increase their ability to identify safety signals earlier.
- To detect safety events that cannot be uncovered in randomized trials (real-life use, off-label use, rare, etc.)

… but generating data does *not* help us provide direct patient care, which is our primary obligation…

Methods

Developing ActionADE

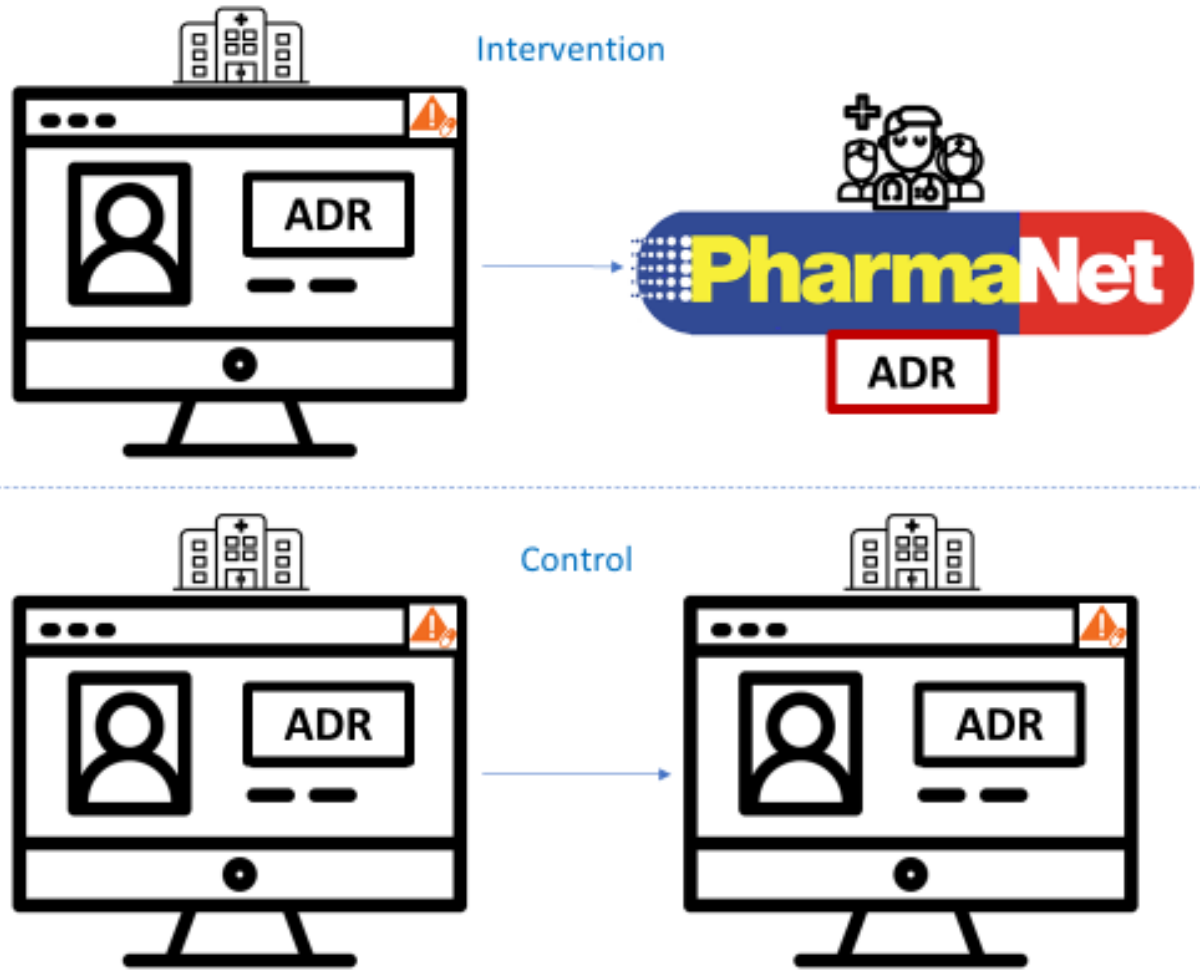


ActionADE

- User-friendly app that you can access and enter data into once you have signed Terms of Use (because we are communicating with PharmaNet)
- Captures clinically relevant information about adverse drug events using a minimum required dataset developed by clinicians
- Allows retrieval and updating of useful and relevant patient and medication-level ADE information to inform future care, and transmits up-to-date information about ADEs to anyone who can access the patient's PharmaNet profile
- Development of community pharmacy alerts in which ADE alerts need to be overridden before culprit medications can be re-dispensed

Try it out during the presentation!
www.actionade.net
physician@actionade.net / Testing123!

Evaluation of effectiveness



- Culprit medication re-dispensation
- Outpatient & ED visits
- Admissions
- Hospital-days
- Mortality
- Costs

Evaluation of Implementation

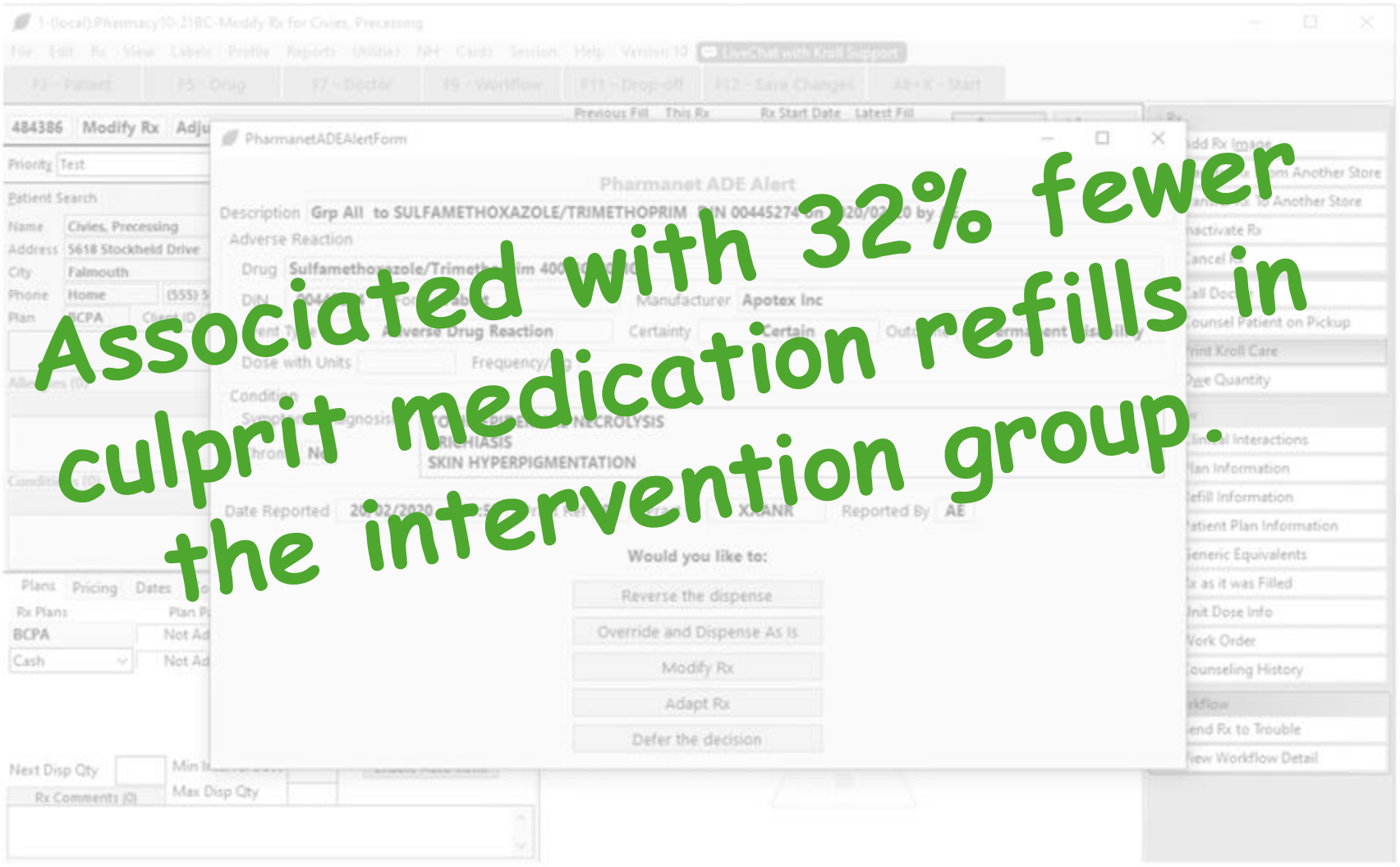
March 2020
ActionADE was launched

275
Users Reporting

6,609
Reports

Data from April 2025

Impact on Safety (intervention group)



Leveraging reported ADE data for surveillance

Our work with the Canadian Drug Agency (CAD)

Canada's Drug and Health Technology Agency

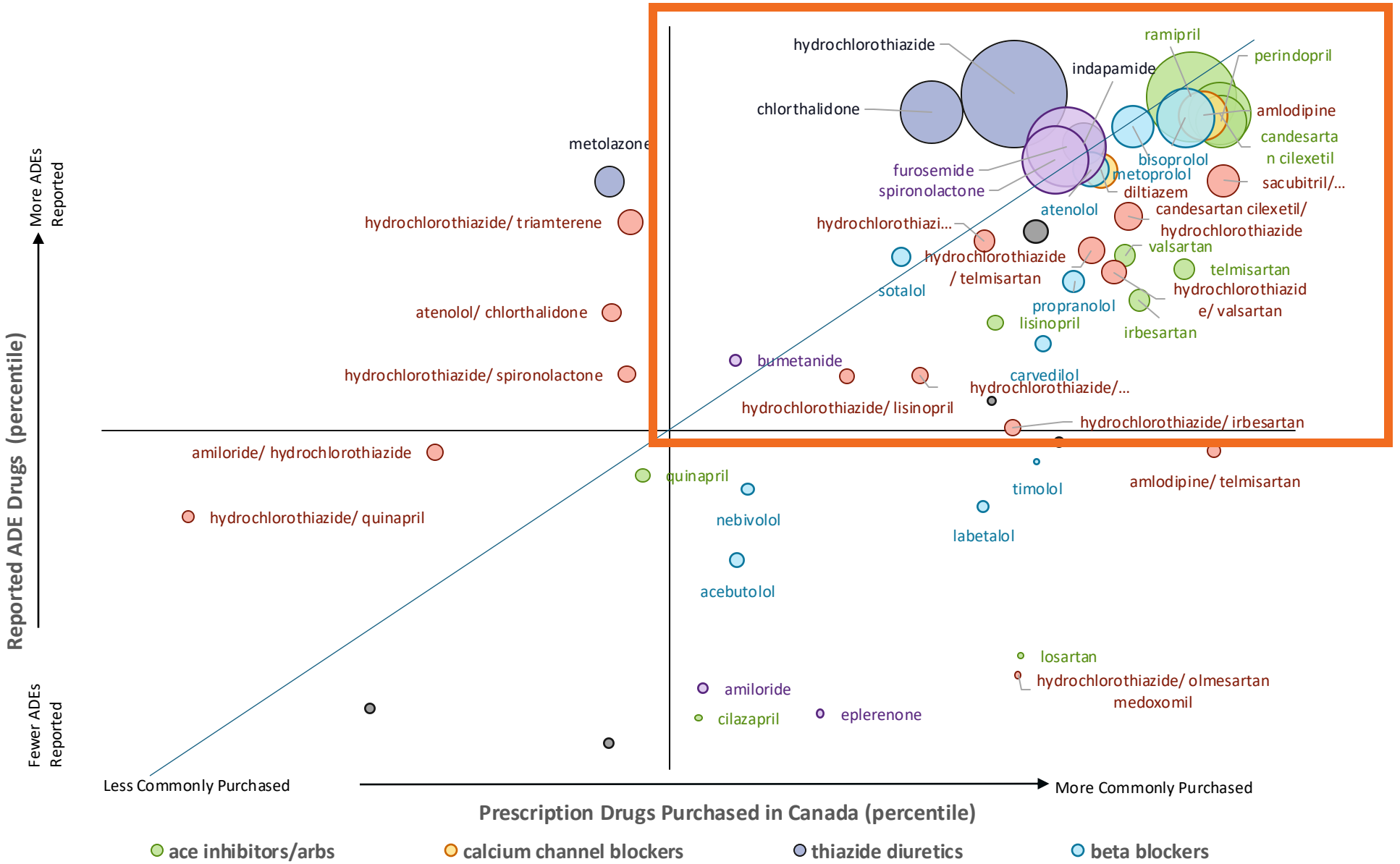
Methods

- Calculate the burden of reported ADEs by multiplying the frequency of reporting * severity (hospitalization, extended hospitalizations, deaths) to obtain percentile rank (least → most burdensome)
- Calculate the percentile rank drug purchasing using national pharmacy data (least → most frequently purchased)
- Identify disproportional percentile ranks to identify concerning safety signals

→ Ecological signals for further investigation in observational studies that may otherwise not have been found

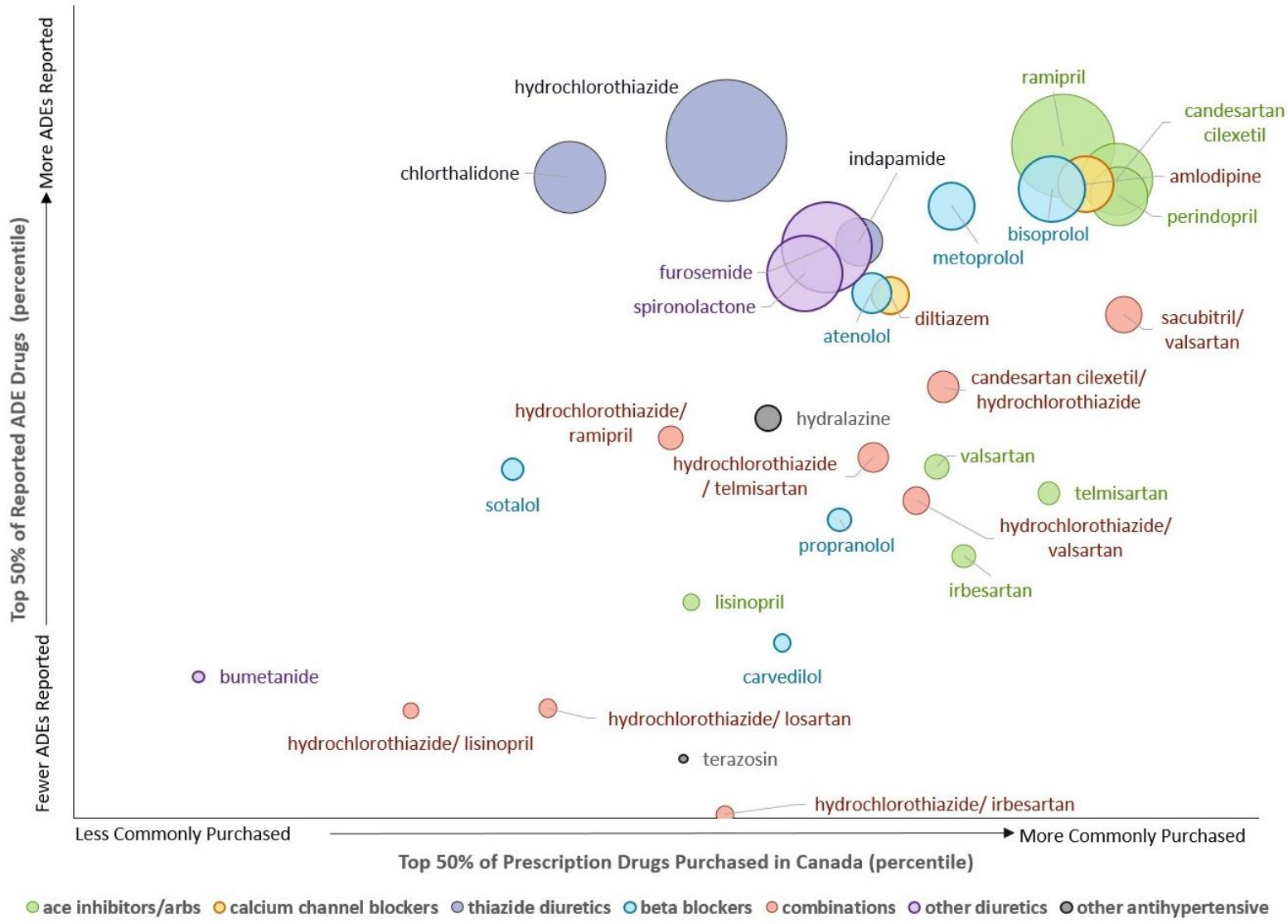
Canada's Drug and Health Technology Agency

ADE report frequency by purchasing frequency of culprit drugs



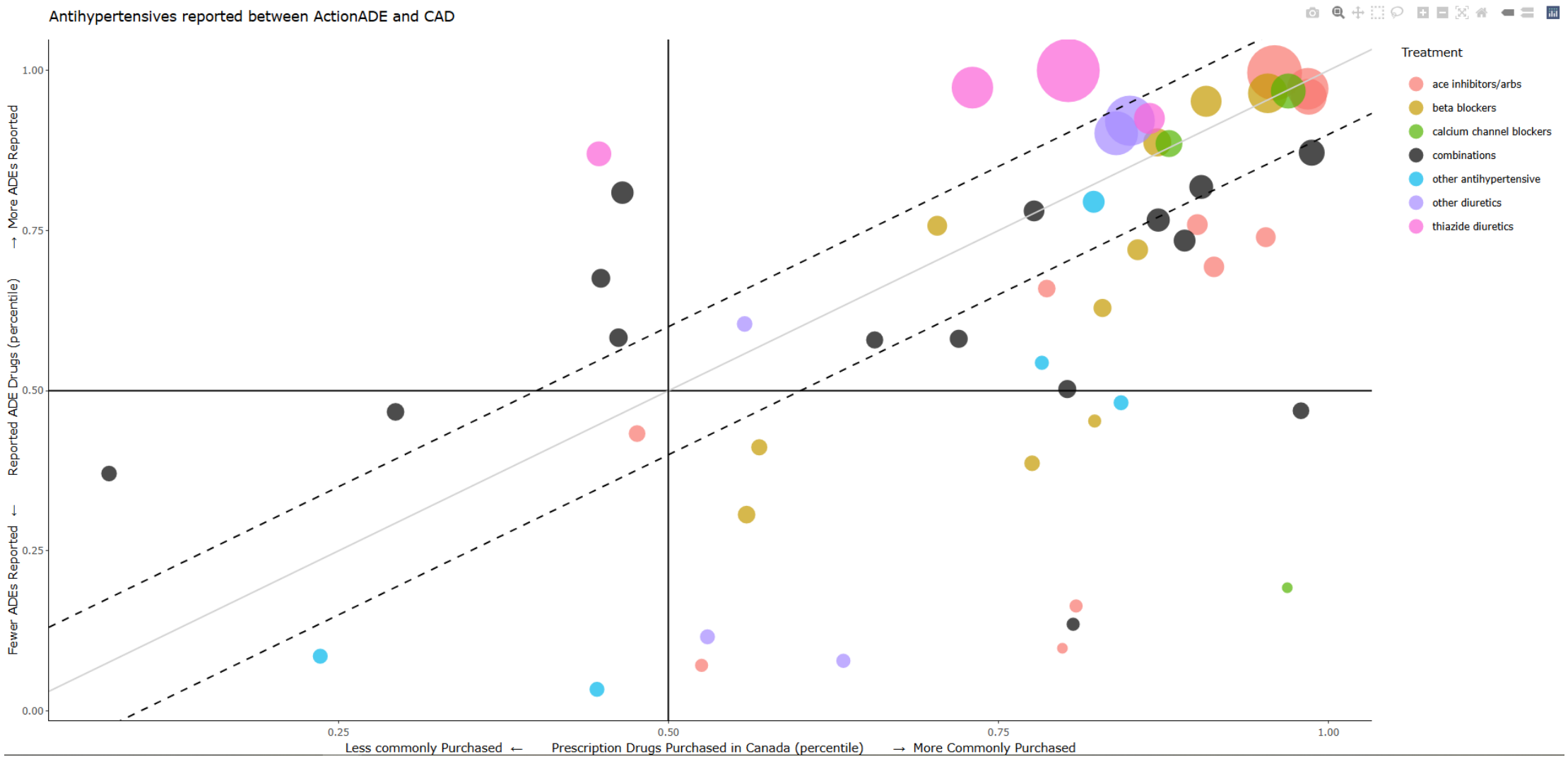
Relative percentiles of ADE report frequency by purchasing frequency of culprit drugs by indication class

ADE report frequency by purchasing frequency of culprit drugs

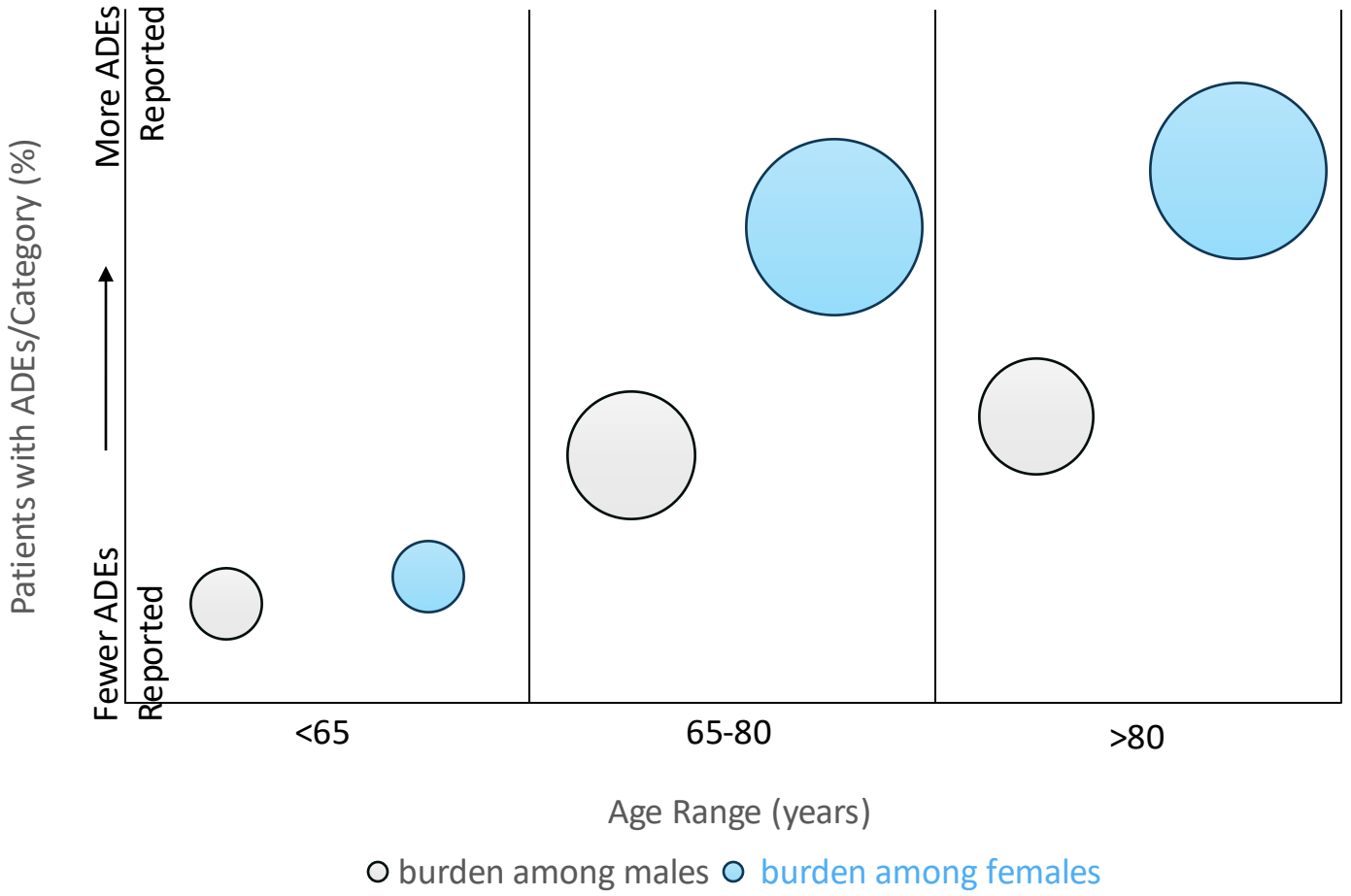


Relative percentiles of reported ADE burden by drug purchasing frequency of culprit drugs classes used for the same treatment indication

Antihypertensive ADE burden versus drug purchasing frequency



Age and sex differences in ADEs due to hydrochlorothiazide



ADE burden of hydrochlorothiazide by age and sex

A H Perspective

Mishell Bareno, SPPH Masters Student

Try the Demo Site:
www.actionade.net
physician@actionade.net / Testing123!

Thank You!

Please contact us if you have any questions or would like to collaborate: actionade.support@ubc.ca

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