US ARMY
PHARMACOVIGILANCE CENTER

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Director
26 May 2011

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US ARMY PHARMACOVIGILANCE CENTER
SIGNAL DETECTION, EVALUATION & PREVENTION

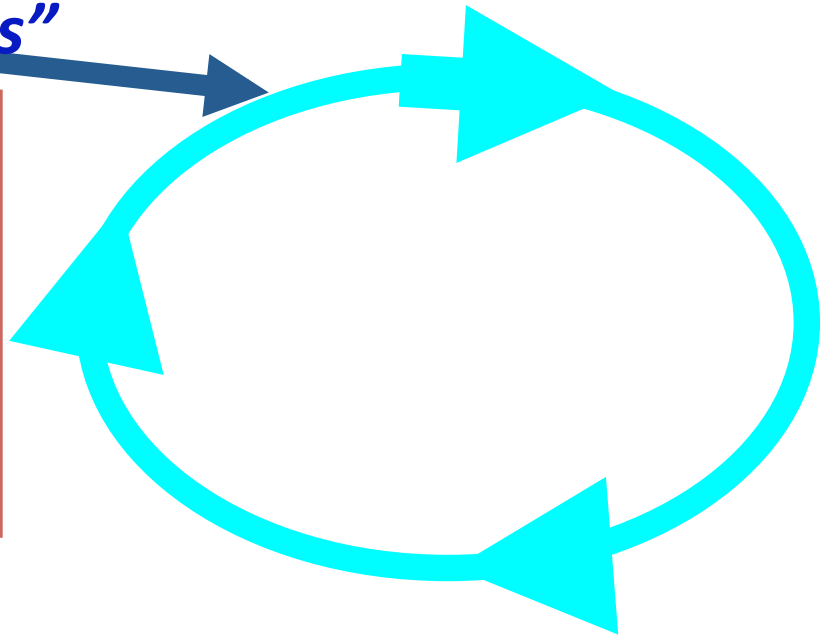
Process of Pharmacovigilance

Formulary: Safe, Effective & Favorable Risk/Benefit Ratio

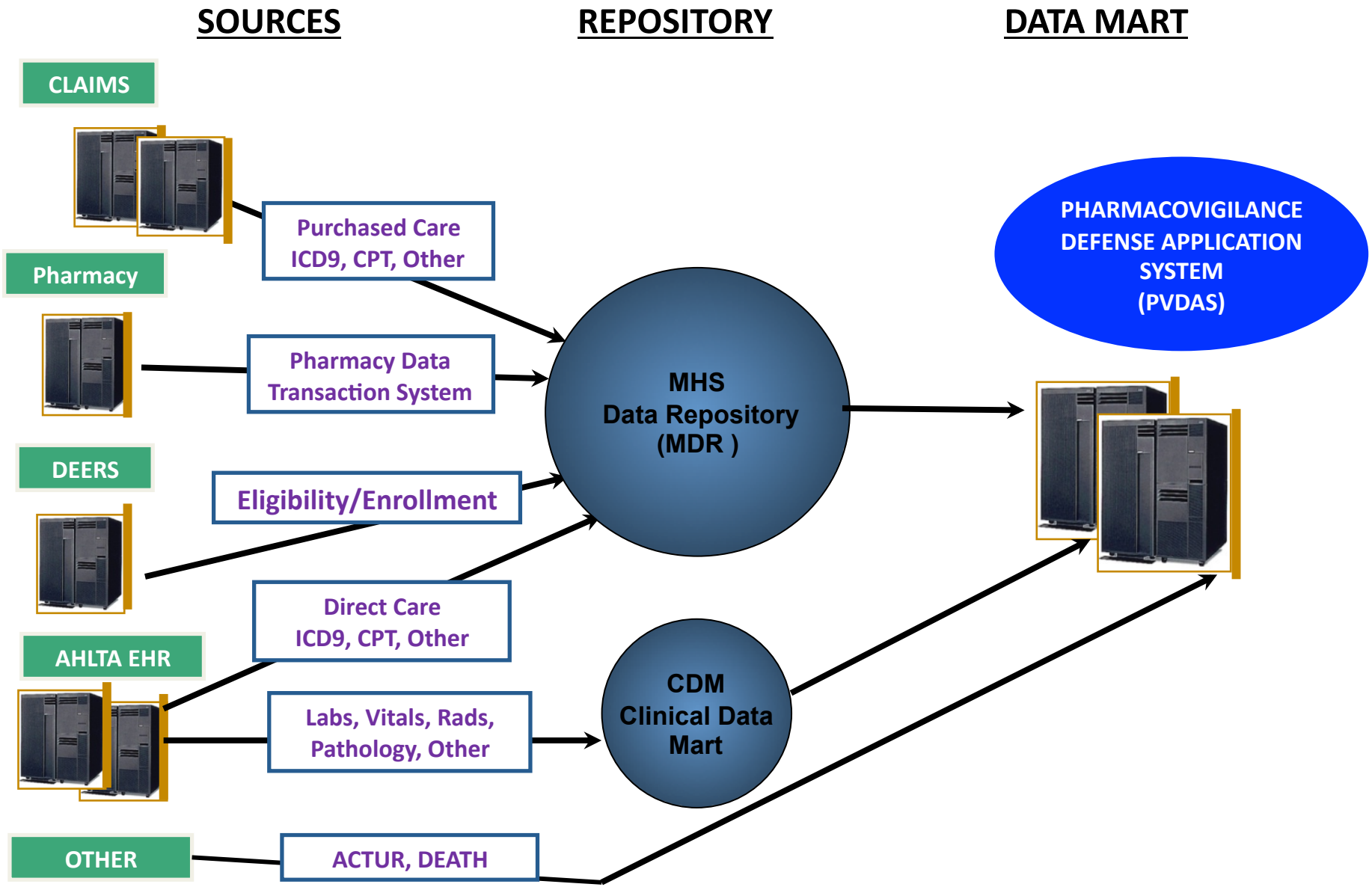
Signal Generation

"Rapid Analysis"

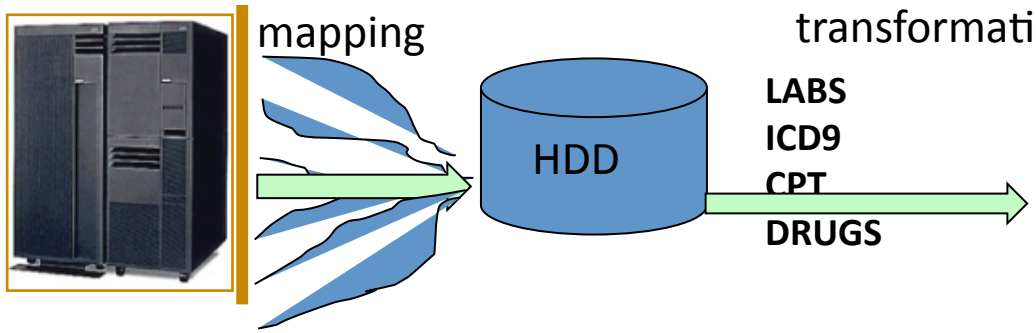
- Signal generated by comparing study drug to comparator drug with similar indications
- Federal Partners Collaboration (FDA, DoD, VHA, CMS) A distributed system using a collaborative active surveillance protocol (incident user design): Dronedarone, Dabigatran



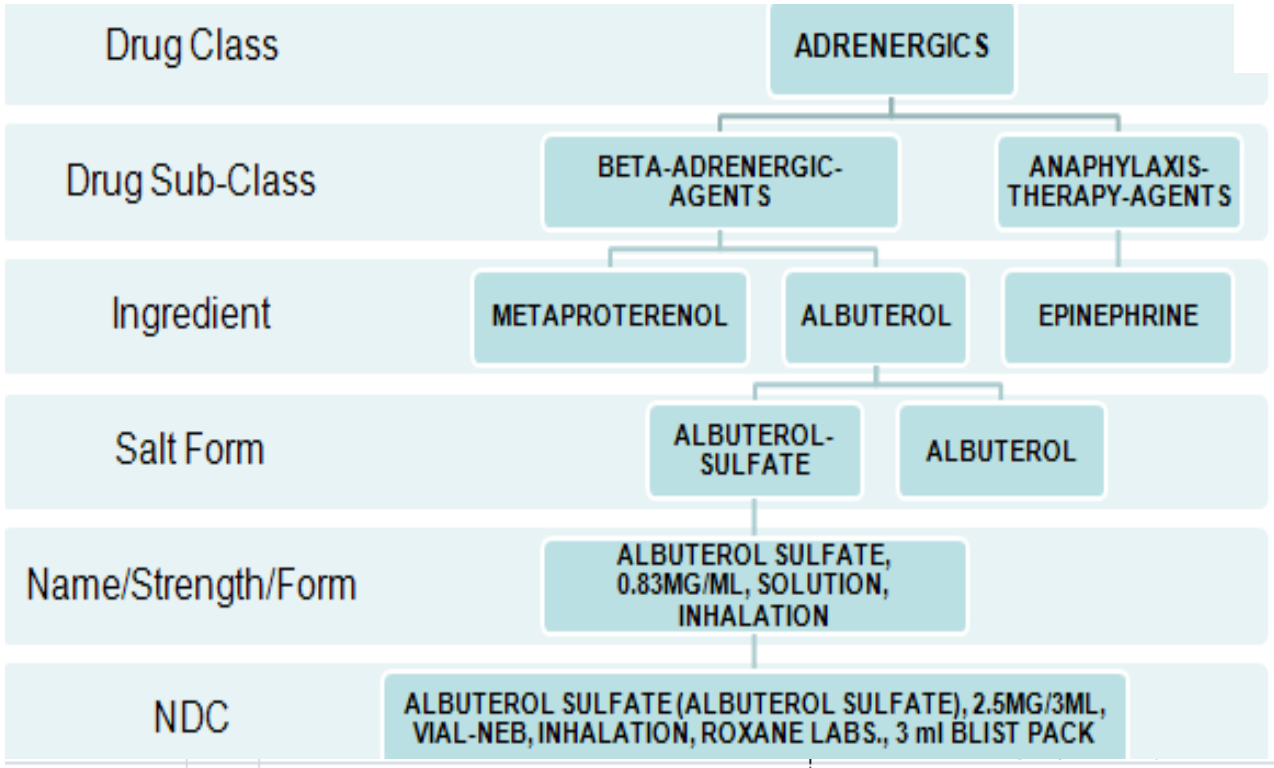
Data Extraction



Data Cleaning and Standardization



- Direct-care diagnostic events and purchased care claims are both coded in ICD-9-CM
- All drugs are coded in NDC
- Queries can be run at any level of the ICD-9-CM hierarchy for events or the AHFS or FDB hierarchies for drugs



GLUCOSE	21	GlucoseMcncPtPcarQn	A Lab Observation Id (552): Glucose, Pericardial Fluid Quantitative
GLUCOSE	16	GlucoseMcncPtBldcoQnGluChem	A Lab Observation Id (552): Glucose, Cord Blood Quantitative
GLUCOSE	8	GlucoseMcncPtBldmvQnGluChem	A Lab Observation Id (552): Glucose, Mixed Venous Blood Quantitative
GLUCOSE	5997	GlucoseMcncPtBldvQnGluChem	A Lab Observation Id (552): Glucose, Blood, Venous Quantitative

Descriptive Analysis

A descriptive analysis generates a variety of counts and other statistics for specified drugs and events occurring in a specified temporal pattern. There are four types:

- Disease Characterization Analysis: computes period prevalence for the occurrence of events of interest across the defined study period

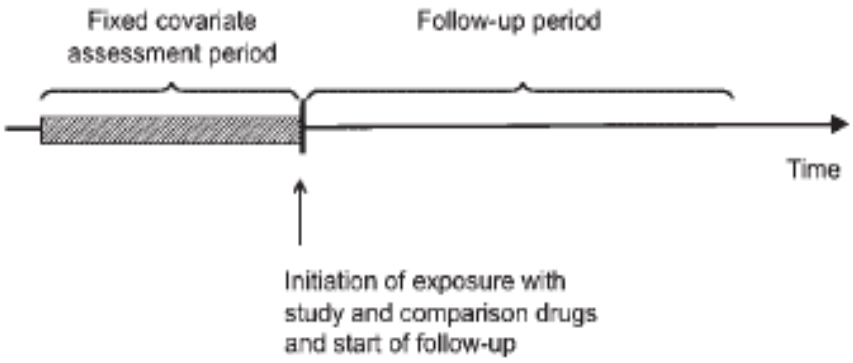
- Drug Utilization Analysis: computes period prevalence for exposure to drugs of interest across the defined study period

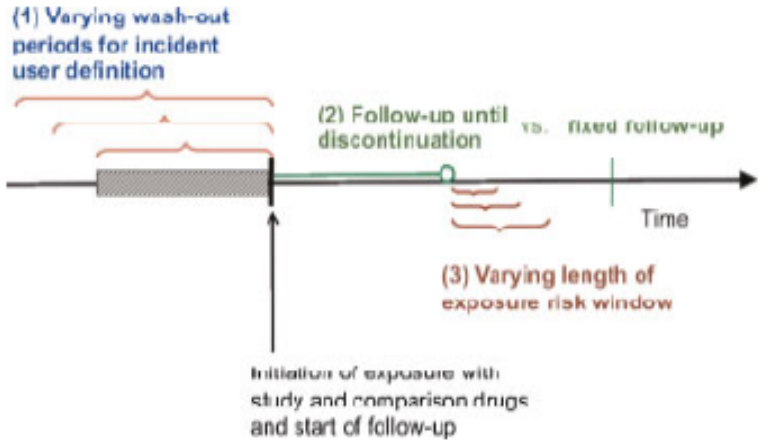
- Risk-outcome Analysis: computes period prevalence and incidence rate for drugs or events of interest during a risk period that one defines based on other drugs or events. For example, you could look at the outcome of hypertension during exposure to an anti-diabetic medication, the outcome of switching to Drug B following the last exposure to Drug A, or the outcome of exposure to Drug C following a particular diagnosis

- Mother-child Analysis: identifies likely pregnancies and the child records associated with them

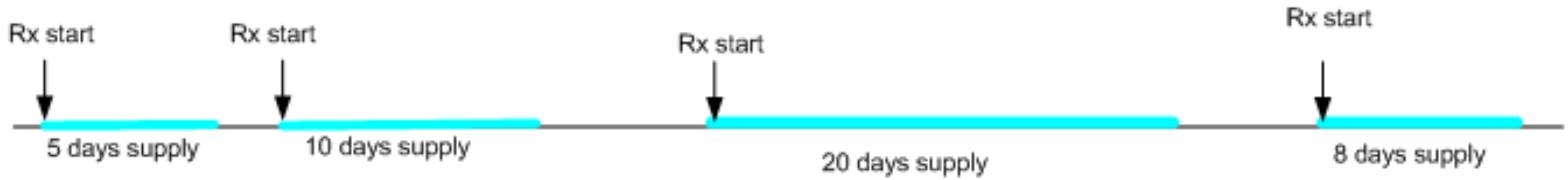
Exploratory Analysis

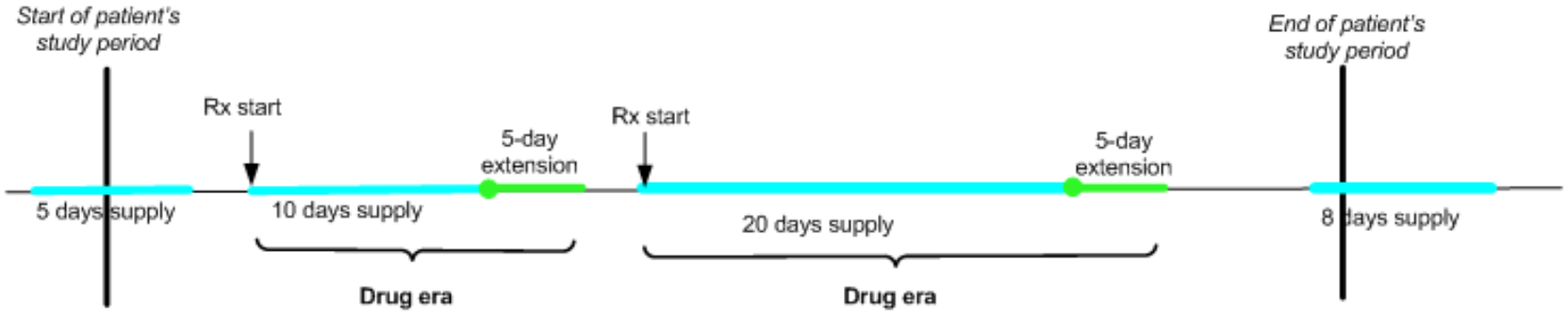
- PVDAS computes an age and gender-stratified relative risk by applying an exposure-based incident (or persistent) user cohort analysis to the drug (or drugs) of interest and a comparator (or unexposed group). Relative risk calculation is based on person-days of follow-up.
- As a comparator, you can use occurrence of the event during non-exposure to the drug or occurrence of the event during exposure to a different drug (or drugs).
- PVDAS exploratory analysis algorithm uses some of the concepts presented in the article: Brown JS et. al. Early detection of adverse drug events within population-based health networks; application of sequential testing methods. *Pharmacoepidemiology and Drug Saf.* 2007 Dec;16(12):1275-84.



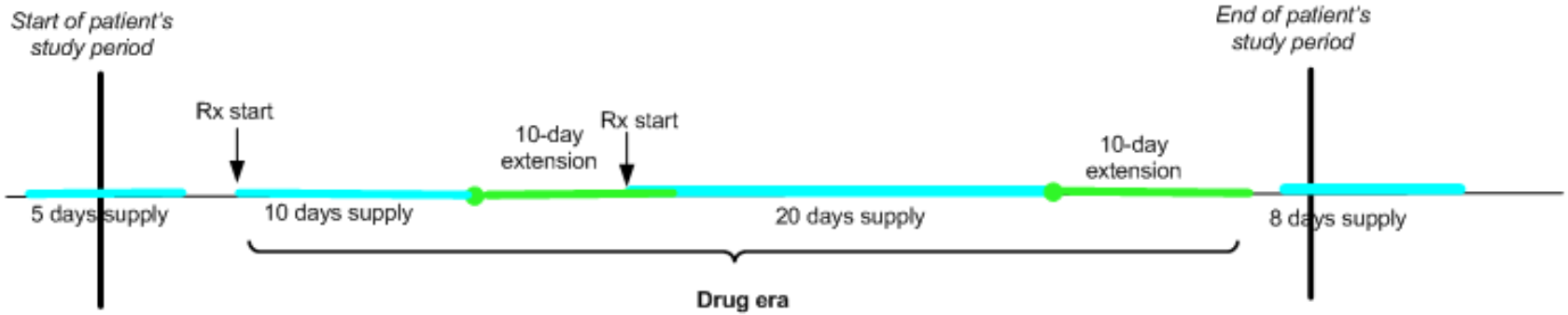


Building Drug Era





The following example shows an exposure extension of 10 days added to each prescription that starts within the patient's study period. exposures that constitute one drug era.



SUMMARY RESULTS OF ALL COMPARISONS

DRUG OF INTEREST (DOI)	OUTCOME	COMPARATOR (C)	SUBSET	N WITH EVENT EXPOSED TO DOI (DOI N)	N WITH EVENT EXPOSED TO C OR UNEXP (C N)	N EXPOSED TO DOI	N EXPOSED TO C OR UNEXPOSED	RRISK_C	RRISK_B	RRISK_B05	RRISK_B95
D&EE	DVT/PE INPAT	unexposed	18-24	8	78	34,999	487,204	5.24	2.84	1.54	4.81
D&EE	DVT/PE INPAT	unexposed	all	18	547	81,111	1,423,020	2.61	2.25	1.49	3.27
D&EE	DVT/PE INPAT	unexposed	25-34	7	147	31,170	368,478	1.94	1.61	0.84	2.80
D&EE	DVT/PE INPAT	unexposed	35-44	3	315	11,130	386,579	1.73	1.34	0.53	2.82
D&EE	DVT/PE INPAT	EE&N	25-34	8	5	40,527	59,382	2.53	1.94	1.05	3.29
Lisinopril	9951:Angioedema	Amlodipine	F|65+	373	62	99,188	49,420	2.48	2.46	2.25	2.68
ACE	9951:Angioedema	CCB	F|65+	245	77	87,894	62,667	2.30	2.28	2.05	2.53

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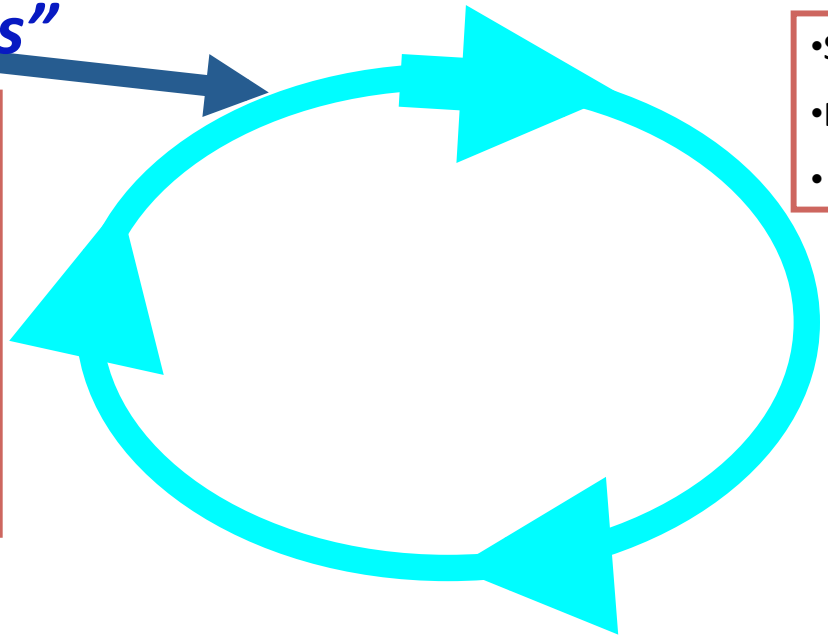
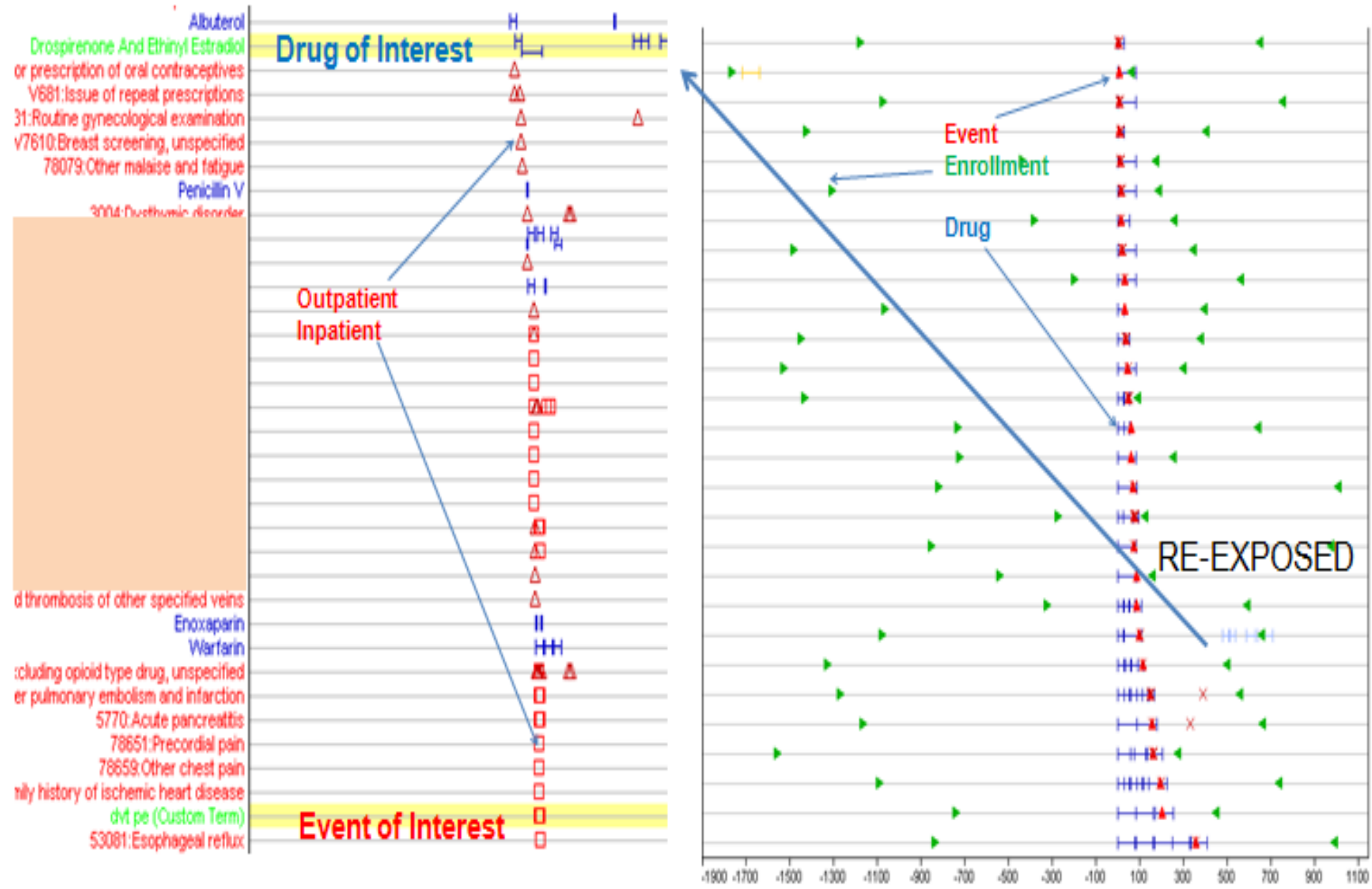


Signal Strengthening

- Subgroup analysis
- Balancing patient characteristics
- Drill into patient timelines


Albuterol
Drospirenone And Ethinyl Estradiol
or prescription of oral contraceptives
V681:Issue of repeat prescriptions
31:Routine gynecological examination
v7610:Breast screening, unspecified
78079:Other malaise and fatigue
Penicillin V
d thrombosis of other specified veins
Enoxaparin
Warfarin
:cluding opioid type drug, unspecified
er pulmonary embolism and infarction
5770:Acute pancreatitis
78651:Precordial pain
78659:Other chest pain
nily history of ischemic heart disease
dvt pe (Custom Term)
53081:Esophageal reflux
Drug of Interest
Outpatient
Inpatient
Event of Interest
Event
Enrollment
Drug
RE-EXPOSED
-1900 -1700 -1500 -1300 -1100 -900 -700 -500 -300 -100 100 300 500 700 900 1100

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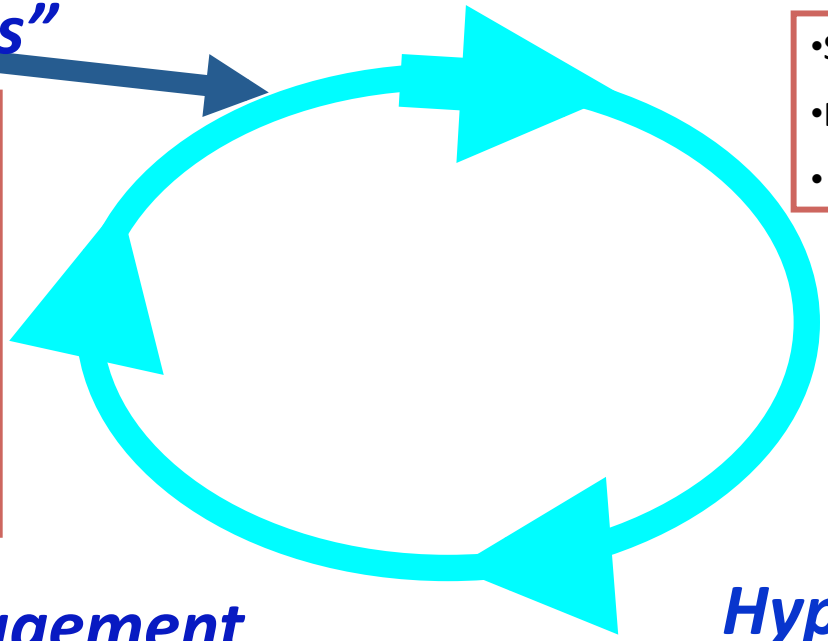


Risk Management

Formulary Decisions & Policy: Mefloquine

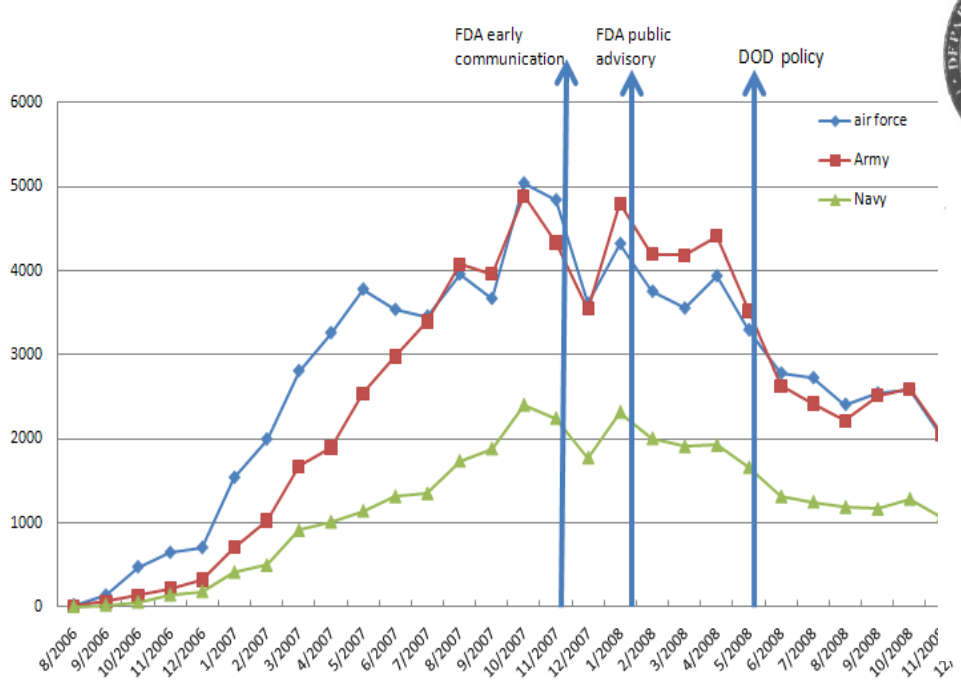
Education Campaign: *Know Your Dose Campaign*

Identification: of drug interactions (tamoxifen and strong CYP enzyme inhibitors)

Hypothesis Testing

Full observational epidemiological study with chart review to validate endpoint

Number of Chantix Scripts Over Time (Three Services)



OFFICE OF THE ASSISTANT SECRETARY OF DEFENSE
WASHINGTON, DC 20301-1200

HEALTH AFFAIRS

SEP 04 2009

MEMORANDUM FOR ASSISTANT SECRETARY OF THE ARMY (M&RA)
ASSISTANT SECRETARY OF THE NAVY (M&RA)
ASSISTANT SECRETARY OF THE AIR FORCE (M&RA)
DIRECTOR OF THE JOINT STAFF

SUBJECT: Policy Memorandum on the Use of Mefloquine (Lariam®) in Malaria Prophylaxis

References: (a) Memorandum, MCPO-NCR, November 20, 2003, Subject: Additional Patient Information to Accompany Each Prescription of Mefloquine (Lariam®).

DoD MEDICATION SAFETY NOTICE

Issue 2 – 6 March 2009

Zonisamide (Zonegran)

On 19 Feb 2009, the Food and Drug Administration (FDA) released an FDA Alert on zonisamide (Zonegran). One of a number of newer anticonvulsants, zonisamide has been causally related to metabolic acidosis, particularly in the pediatric age group. Zonisamide is indicated as adjunctive therapy in the treatment of partial seizures in adults.

Controlled Drug Management, Analysis and Reporting Tool (CD-MART) Target Population

- **Focus on beneficiaries enrolled to specific MTF, includes all enrollment locations under the MTF commander**
- **Data from within the MTF's 40-mile catchment area or all of the Department of Defense (DOD).**
- **All points of service**
- **controlled substances**