RWE and Pharmaceuticals
Challenges and Approach

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PRISME
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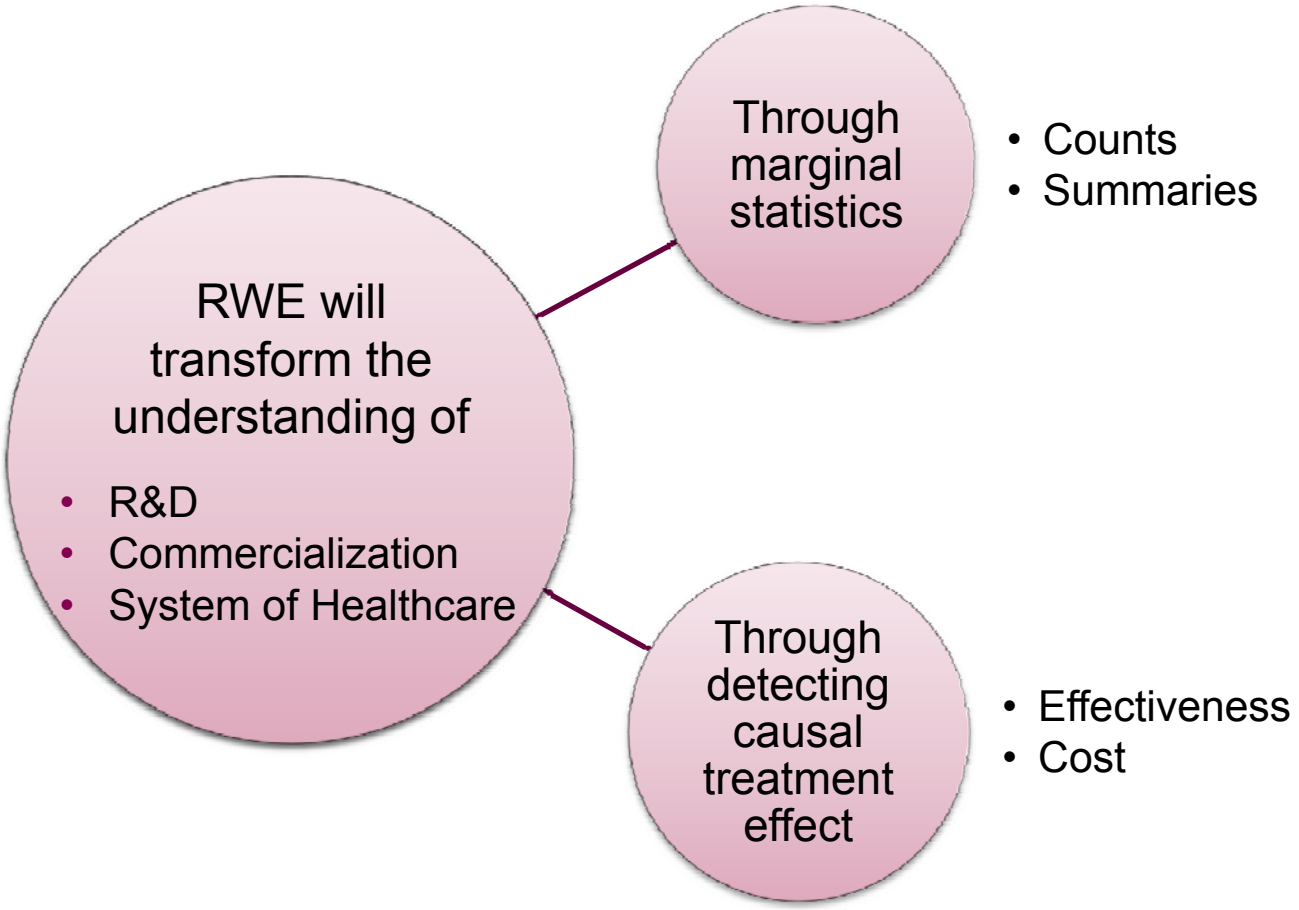
Insights from RWE
Opportunities and Application



Assumption

We know exactly how to do it and we will find the insights

BMJ 2010; 341:c4444

BMJ

RESEARCH

Oral bisphosphonates and risk of cancer of oesophagus, stomach, and colorectum: case-control analysis within a UK primary care cohort

Jane Green, clinical epidemiologist,[1] Gabriela Czanner, statistician,[1] Gillian Reeves, statistical epidemiologist,[1] Joanna Watson, epidemiologist,[1] Lesley Wise, manager, Pharmacoepidemiology Research and Intelligence Unit,[2] Valerie Beral, professor of cancer epidemiology[1]

ORIGINAL CONTRIBUTION

JAMA 2010; 304(6): 657-663

JAMA®

Exposure to Oral Bisphosphonates and Risk of Esophageal Cancer

Chris R. Cardwell, PhD
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Marie M. Cantwell, PhD
Liam J. Murray, MD

Context Use of oral bisphosphonates has increased dramatically in the United States and elsewhere. Esophagitis is a known adverse effect of bisphosphonate use, and recent reports suggest a link between bisphosphonate use and esophageal cancer, but this has not been robustly investigated.

Objective To investigate the association between bisphosphonate use and esoph-

BMJ Results

Table 2 | Relative risks (RRs) and 95% confidence intervals (CIs) for bisphosphonates

Oral bisphosphonates	Oesophagus		
	Prescriptions*	Cases/controls	RR† (95% CI)
Not prescribed	NA	2864/14 376	1.00
Prescribed	13.6/2.4	90/345	1.30 (1.02 to 1.66)
No of prescriptions:			
1-9	3.6/1.0	40/214	0.93 (0.66 to 1.31)
≥10	21.6/3.5	50/131	1.93 (1.37 to 2.70)
Estimated duration of use‡:			
≤1 year	4.9/0.3	31/155	0.98 (0.66 to 1.46)
1-3 years	13.0/2.0	26/114	1.12 (0.73 to 1.73)
≥3 years	22.2/4.6	33/76	2.24 (1.47 to 3.43)

NA=not applicable.
*Prescriptions of bisphosphonates in cases; reported as mean number/mean ye
†All relative risks adjusted for smoking status, alcohol intake, and body mass in
‡Time between first and last prescription.

Conclusions The risk of oesophageal cancer increased with 10 or more prescriptions for oral bisphosphonates and with prescriptions over about a five year period. In

JAMA Results

dence in the Bisphosphonate and Matched Control Cohorts

Bisphosphonate		Control		Risk			
				Unadjusted		Adjusted[a]	
Cases	Person-Years	Cases	Person-Years	HR (95% CI)	*P* Value	HR (95% CI)	*P* Value
79	165 400	72	163 480	1.08 (0.79-1.49)	.63	1.07 (0.77-1.49)	.67
51	104 676	49	104 104	1.04 (0.70-1.53)	.86	1.05 (0.70-1.57)	.82
31	73 364	35	73 170	0.88 (0.55-1.43)	.62	0.92 (0.56-1.51)	.74
22	40 326	22	40 492	1.00 (0.56-1.81)	.99	0.98 (0.53-1.81)	.95
15	22 813	14	22 891	1.08 (0.52-2.23)	.84	1.01 (0.48-2.12)	.99
35	62 922	27	63 648	1.31 (0.80-2.17)	.29	1.24 (0.74-2.09)	.41
24	58 162	23	55 334	0.98 (0.55-1.74)	.94	1.03 (0.57-1.86)	.92
20	44 316	22	44 497	0.91 (0.50-1.67)	.78	0.90 (0.48-1.68)	.74
44	106 480	47	106 412	0.94 (0.62-1.41)	.75	0.96 (0.63-1.47)	.86
30	70 251	34	69 935	0.88 (0.54-1.44)	.61	0.93 (0.56-1.54)	.78
22	39 022	22	39 187	1.01 (0.56-1.82)	.99	0.98 (0.53-1.80)	.95
33	81 369	42	80 837	0.78 (0.50-1.23)	.29	0.77 (0.48-1.23)	.27
22	52 308	31	51 741	0.70 (0.41-1.21)	.20	0.68 (0.39-1.19)	.18
19	28 898	21	28 904	0.91 (0.49-1.68)	.75	0.85 (0.45-1.61)	.62
35	58 920	25	57 068	1.35 (0.81-2.25)	.25	1.25 (0.73-2.12)	.37

Conclusion Among patients in the UK General Practice Research Database, the use of oral bisphosphonates was not significantly associated with incident esophageal or gastric cancer.

Assumption

We can treat RWE like Clinical Trials

We know how to run RWE because we know clinical studies

Clinical study = roughly equivalent to RWE

- Cut data: Inclusion and exclusion criteria
- Treatment, control arm Create cohorts/cases
- Detect "end points": Algorithms for outcomes
- Remove bias: Adjust for confounding
- Reject null hypothesis: Calculate *p*-value
- Do it correctly: Use existing machinery and governance

Typical inclusion/exclusion criteria

Open-label Study of TH-302 and Dexamethasone With or Without Bortezomib in Subjects With Relapsed/Refractory Multiple Myeloma

Inclusion Criteria:

- At least 18 years of age.
- Ability to understand the purposes and risks of the study and has signed a written informed consent form approved by the investigator's IRB/Ethics Committee.
- Relapsed/refractory multiple myeloma for which no standard therapy options are anticipated to result in a durable remission.
- Subjects with refractory disease are allowed to participate on study. (Refractory disease is defined as progressive disease within 60 days of last therapy or progression while on therapy).
- Receipt of at least two prior therapies (induction therapy with stem cell transplant with or without maintenance is considered a prior therapy) including prior therapy with a bortezomib-containing regimen (and did not discontinue due to toxicity) and a lenalidomide- or thalidomide-containing regimen
- Subjects with measurable disease defined as at least one of the following:
- Serum M-protein ≥ 0.5 mg/dl
- Urine M-protein ≥ 200 mg/24 h
- Serum FLC assay: Involved FLC level ≥ 10 mg/dl (≥ 100 mg/l)
- Measurable plasmacytoma (should be measured by CT or PET/CT within 28 days of initial investigational agent dosing).
- ECOG performance status of less than or equal to 2 (see Appendix B)
- Acceptable liver function:
- Total bilirubin ≤ 1.5 times upper limit of normal (x ULN). If total bilirubin is elevated, check direct and if normal then the subject is eligible
- Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≤ 3.0 x ULN (≤ 5.0 x ULN if due to myeloma involvement).
- Alkaline phosphatase ≤ 3.0 x ULN (≤ 5.0 x ULN if due to leukemic involvement)
- Acceptable renal function:
- Serum creatinine ≤ 1.5 x ULN or calculated creatinine clearance above 40 mL/min using the formula of Cockcroft and Gault, or a 24 hr creatinine clearance if borderline
- Acceptable hematologic status (without hematologic support):
- ANC ≥ 1000 cells/μL (growth factors may not be used within 7 days prior to evaluation)
- Platelet count ≥ 75,000/μL (for subjects in whom < 50% of bone marrow nucleated cells are plasma cells); platelet count > 50,000/μL for subjects in whom ≥ 50% of bone marrow nucleated cells are plasma cells (without transfusion during the previous 14 days prior to evaluation)
- Hemoglobin ≥ 8.0 g/dL (without transfusion during the previous 14 days prior to evaluation).
- All women of childbearing potential must have a negative serum pregnancy test and women and men subjects must agree to use effective means of contraception (surgical sterilization or the use or barrier contraception with either a condom or diaphragm in conjunction with spermicidal gel or an IUD) with their partner from entry into the study through 6 months after the last dose
- Subjects must adhere to the study visit schedule and other protocol requirements and receive outpatient therapy and laboratory monitoring at the institute that administers the study drug.

Exclusion Criteria:

- Subjects with non secretory or hyposecretory MM
- POEMS syndrome (polyneuropathy, organomegaly, endrocintopathy, monoclonal gammothy and skin changes.
- Plasma cell leukemia
- Waldnestrom's macroglobinemia
- Subject with known or suspected amyloidosis
- Corticosteroid therapy in a dose equivalent to dexamethasone > 1.5 mg/day or prednisone > 10 mg/day within 2 weeks prior to first dose, Subjects may be receiving chronic corticosteroids if they are being given for disorders other than multiple myeloma if they meet the above
- Planned radiation therapy that occurs after the start of therapy
- Localized radiation therapy to only measurable disease site(s) within 4 weeks of treatment
- New York Heart Association (NYHA) Class III or IV, cardiac disease, myocardial infarction within 6 months prior to Day 1, or unstable arrhythmia
- Significant neuropathy (Grade 3 or 4, or Grade 2 with pain) at the time of enrollment or within 14 days before enrollment
- Symptomatic brain metastases (unless previously treated and well controlled for a period of ≥ 3 months)
- Severe chronic obstructive pulmonary disease with hypoxemia or in the opinion of the investigator any physiological state leading to hypoxemia
- Major surgery, other than diagnostic surgery, within 4 weeks prior to Day 1, without complete recovery
- Active, uncontrolled bacterial, viral, or fungal infections, requiring systemic therapy within 14 days prior to the first dose
- Previously treated malignancies, except for adequately treated non-melanoma skin cancer (basal cell or squamous cell), in situ cancer, or other cancer from which the subject has been disease-free for at least 5 years
- Subjects who participated in an investigational drug or device study within 2 weeks prior to study entry
- Known or suspected active infection with HIV, hepatitis A, hepatitis B, or hepatitis C
- Subjects who have exhibited allergic reactions to a similar structural compound, biological agent, or formulation similar to TH-302, bortezomib or pimonidazole
- Females who are pregnant or breast-feeding
- Concomitant psychiatric disease or medical condition that could interfere with the conduct of the study, or that would, in the opinion of the investigator, pose an unacceptable risk to the subject in this study
- Unwillingness or inability to comply with the study protocol for any reason
- All previous cytotoxic therapies for multiple myeloma must have been completed at least 3 weeks prior to start of study. Biologic, novel therapy or corticosteroids must have been completed at least 2 weeks prior to start of study.
- Subjects who have been on hormone replacement less than 2 months (subjects on hormone replacement for at least 2 months will not be excluded provided the HRT regimen remains unchanged during the conduct of the study).
- Prior peripheral stem cell transplant within 12 weeks of the start of study
- Epilepsy or other convulsive disorder requiring active management

Comparator Selection

- **All patients**
- **All patients but treated**
- **Matched patients by co-variates**
  - Age
  - Gender
  - Co-morbidity
  - Conmediation
  - Smoking status
- **Pick co-variates manually/automatically**
- **Treat missing data**

Algorithms for Outcomes: Acute Renal Failure

Citation	Diagnosis Codes	Procedure Codes	Laboratory Results
Beard K, Perera DR, Jick H. Drug-induced parenchymal renal disease in outpatients. J Clin Pharmacol. May 1988;28(5):431-435.	For newly diagnosed parenchymal drug-induced renal disease: • acute renal failure: 5851 • acute glomerulonephritis: 5800 • nephrotic syndrome: 5810 • glomerulonephritis NOS: 5830 • renal sclerosis: 5840 • acute tubular necrosis: 5850 • water-losing nephritis: 5861 • renal failure NOS: 5859 • renal cortical necrosis: 5931 • renal disease NEC: 5935 • oliguria and anuria: 7837	None	None
Evans JM, McGregor E, McMahon AD, McGilchrist MM, Jones MC, White G, McDevitt DG, MacDonald TM .Non-steroidal anti-inflammatory drugs and hospitalization for acute renal failure. QJM. 1995 Aug;88(8):551-7.	• 583.8 • 584.5 • 584.7 • 584.8 • 584.9	None	None
Perez Gutthann S, Garcia Rodriguez LA, Raiford DS, Duque Oliart A, Ris Romeu J. Non-steroidal anti-inflammatory drugs and the risk of hospitalization for acute renal failure. Archives of Internal Medicine. 1996;156:2433-2439.	• 580.9 acute nephritis NOS • 581 nephrotic syndrome • 583.2 membranoproliferative nephritis NOS • 583.6 renal cortical necrosis • 583.7 nephritis NOS with medullary necrosis • 583.8 nephritis NOS with other lesions • 583.9 nephritis NOS39 • 584 acute renal failure • 586 renal failure NOS • 593.9 disorder of kidney and ureter NOS	None	Serum creatinine, BUN or urea increased above normal values
Griffin MR, Yared A, Ray WA. Nonsteroidal anti-inflammatory drugs and acute renal failure in elderly persons. Am J Epidemiol. 2000 Mar 1;151(5):488-96.	• Acute renal failure plus other renal conditions 584, 580-583, 585-589, 403, 404, 250.4, 590.0, 590.8, 274.1, 753.1, 593.9 (page 489)	None	None
Bellomo R, Kellum JA, Ronco C. Defining acute renal failure: physiological principles. Intensive Care Med. Jan 2004;30(1):33-37.			**Risk:** Increased SCreat x 1.5 or GFR decrease > 25%, (OR) Urine output < 0.5ml/kg/h x 6 hr. **Injury:** Increased SCreat x 2 or GFR decrease > 50%, (OR) urine output < 0.5ml/kg/h x 12 hr **Failure:** Increased SCreat x 3, GRF decrease 75%, or SCreat≥4mg/dl (acute rise ≥0.5 mg/dl) (OR) urine output < 0.3ml/kg/h x 24 hr or anuria x 12 hrs **Loss:** Persistent ARF = complete loss of kidney function > 4 weeks
Clinard F, Sgro C, Bardou M, et al. (2004). "Association between concomitant use of several systemic NSAIDs and an excess risk of adverse drug reaction. A case/non-case study from the French Pharmacovigilance system database." Eur J Clin Pharmacol 60(4): 279-83	• 0618	None	None
Wintersteen AC, Weiner ID, Johns TE, Hatton RC	• 584.xx	• Dialysis	Algorithm 2: 50% increase of serum creatinine

Acute Renal Failure – cont.

Winterstein AG, Weiner ID, Johns TE, Hatton RC. Validation of Automated Database Algorithms to Identify Hospital-Acquired Renal Failure. [University of Florida, Gainesville, FL, USA. ISPOR 2004] [Abstract] Value Health 2004 7 (3): PUK13 [, PG. 366].	• 584.xx	• Dialysis	Algorithm 2: 50% increase of serum creatinine (SCr) within 3 days Algorithm 3: 50% SCr decrease between peak and discharge
Cziraky MJ, Willey VJ, McKenney JM, et al. Statin safety: an assessment using an administrative claims database. Am J Cardiol. Apr 17 2006;97(8A):61C-68C.	• 584.xx (acute renal failure/acute tubular necrosis)	None	None
Goettsch WG, Heintjes EM, Kastelein JJP, Rabelink TJ, Johansson S, Herings RMC. Results from a rosuvastatin historical cohort study in more than 45,000 Dutch statin users, a PHARMO study. Pharmacoepidemiol Drug Saf. 2006 Jul;15(7):435-43.	Renal impairment including acute renal failure: • 580.9 • 581.9 • 583.4 • 583.6 • 583.7 • 584 • 586	None	(Baseline) creatinine > ULN (OR) sediment present and low urine volume and blood urea nitrogen >100 mg/dL
Schneider V, Levesque LE, Zhang B, Hutchinson T, Brophy JM. Association of selective and conventional nonsteroidal anti-inflammatory drugs with acute renal failure: A population-based, nested case-control analysis. Am J Epidemiol. Nov 1 2006;164(9):881-889.	• 584 • 586	Not stated	None
Waikar SS, Wald R, Chertow GM, Curhan GC, Winkelmayer WC, Liangos O, Sosa MA, Jaber BL. Validity of International Classification of Diseases, Ninth Revision, Clinical Modification Codes for Acute Renal Failure. J Am Soc Nephrol. 2006 Jun;17(6):1688-94. Epub 2006 Apr 26.	*For acute renal failure:* • 584.5, • 584.6 • 584.7 • 584.8 • 584.9	*For acute renal failure that requires dialysis:* • 39.95 (hemodialysis) • V45.1 (renal dialysis status) • V56.0 (extracorporeal dialysis) • V56.1 (fitting and adjustment of dialysis catheter)	None
McAfee, A. T., E. E. Ming, et al. (2006). "The comparative safety of rosuvastatin: a retrospective matched cohort study in over 48,000 initiators of statin therapy." Pharmacoepidemiol Drug Saf 15(7): 444-53.	Acute renal failure, 584.x; other renal dysfunction, 580.x, 581.x, 583.x, 585.x, 586.x,	ICD-P: 39.95 (hemodialysis), 54.98 (peritoneal dialysis) CPT: 90935-90940 (hemodialysis procedures), 90945-90999 (miscellaneous dialysis procedures).	None
Winkelmayer WC, Waikar SS, Mogun H, Solomon DH. Nonselective and cyclooxygenase-2-selective NSAIDs and acute kidney injury. Am J Med. Dec 2008;121(12):1092-1098.	• 584.5 • 584.6 • 584.7 • 584.8 • 584.9	None	None

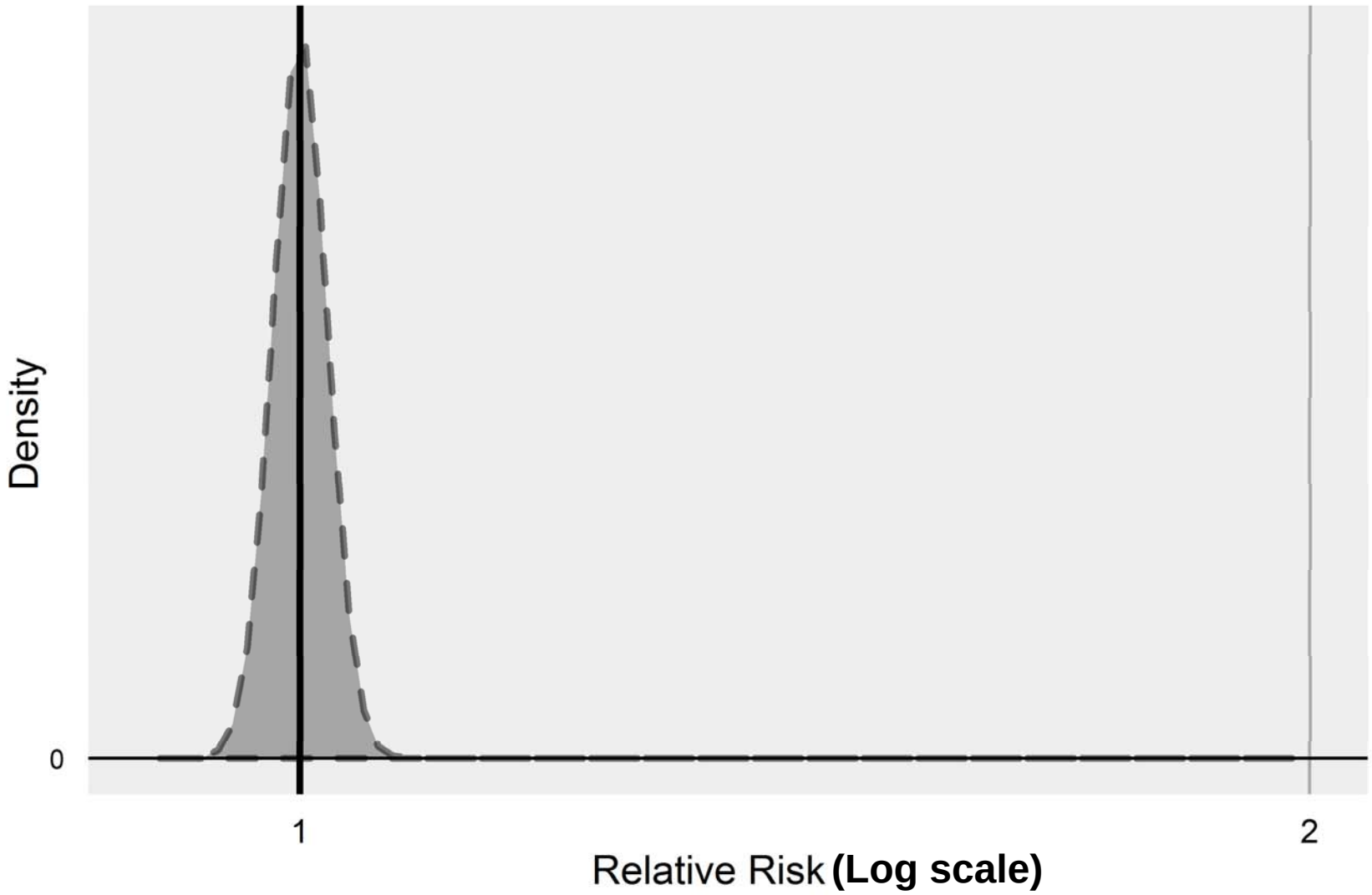
Value of *p*-value

Typical GI study

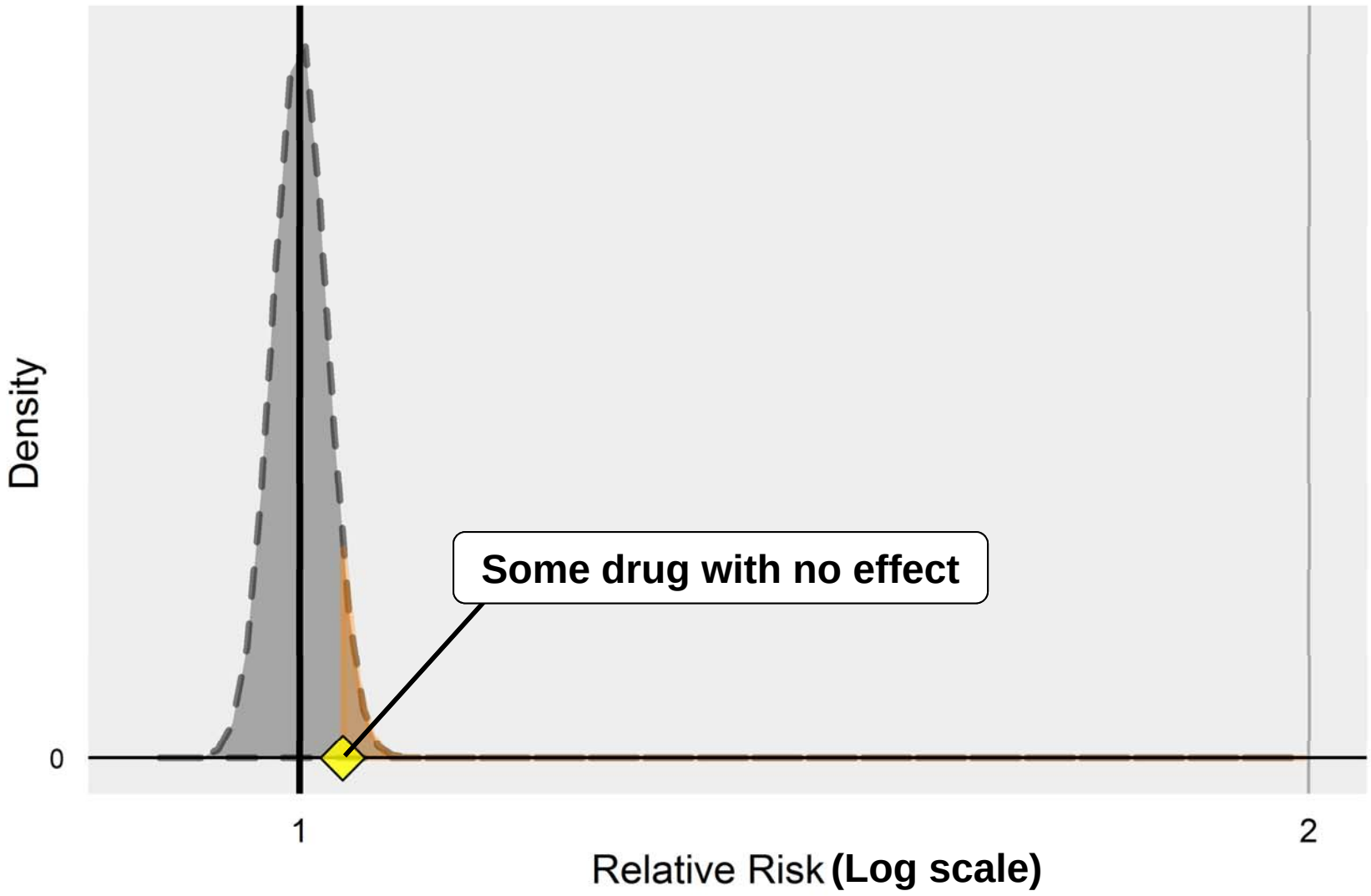
- Opatrny et al., Br J Clin Pharmacol Jul 2008
- Data source: General Practice Research Database
- Study design: Case-control Case definition:
- First episode of upper GI hemorrhage 10 controls per case, matched on index date, age, and practice
- Exposure definition: Prescription issues in 90 days before index date
- Exclusion criteria: < 3 years of observation
- "RR" estimated with conditional logistic regression
- Covariates: sex, BMI, BP, smoking, comorbidities, concomitant medications

Agent	Cases (*n* = 4028)	Controls (*n* = 40 171)	Crude rate ratio	Adjusted rate ratio*	95% confidence interval
Antidepressants					
SSRI	335 (8.3%)	1780 (4.4%)	1.97	1.33	1.09, 1.62
TCA	262 (6.5%)	1764 (4.4%)	1.52	1.04	0.83, 1.30
Venlafaxine	56 (1.4%)	229 (0.6%)	2.48	1.85	1.34, 2.55
Anticoagulant					
Warfarin	281 (7.0%)	1130 (2.8%)	2.64	2.17	1.82, 2.59
Clopidogrel	160 (4.0%)	532 (1.3%)	3.16	2.07	1.66, 2.58

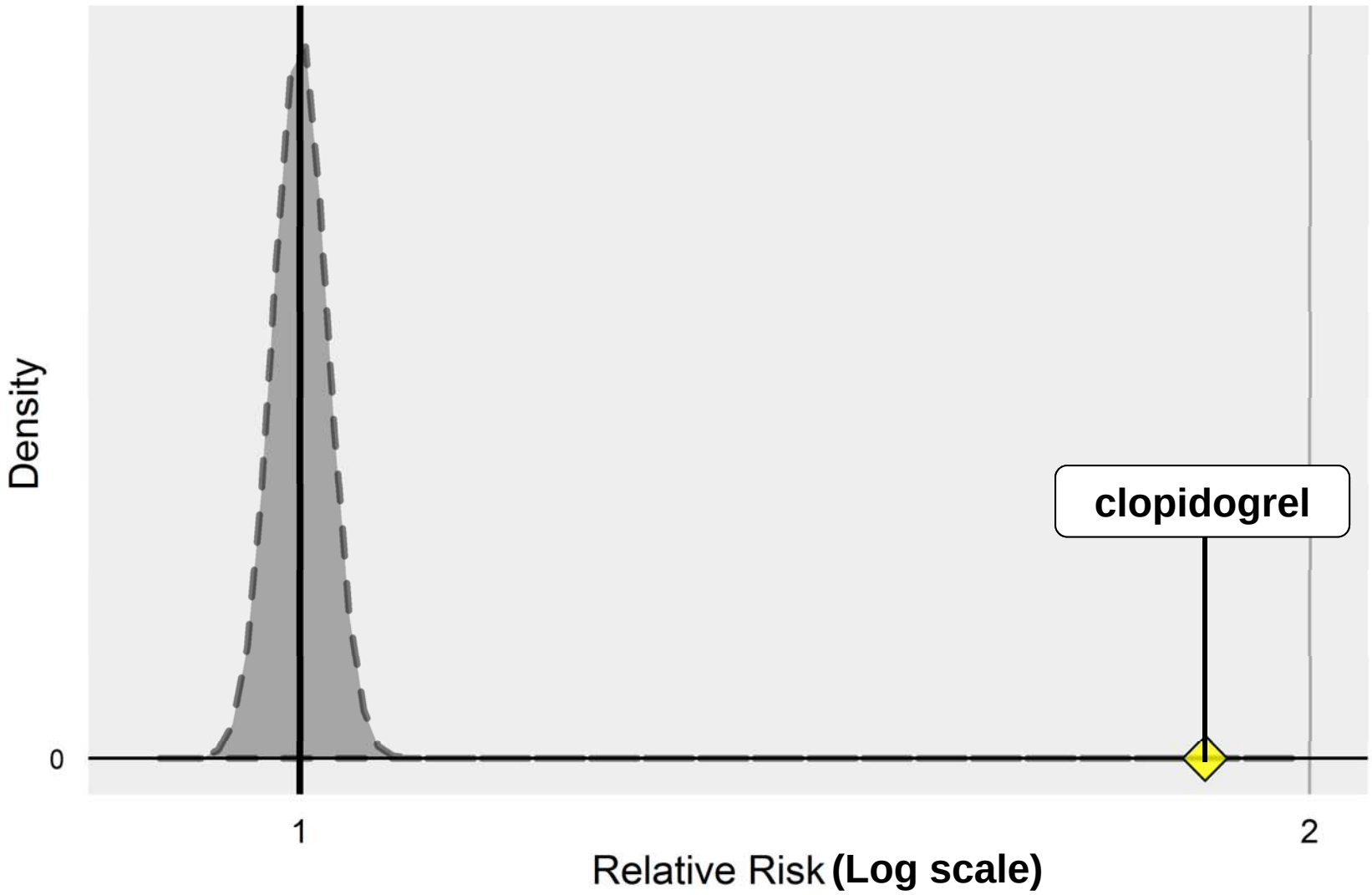
Null distribution



Null distribution



Null distribution



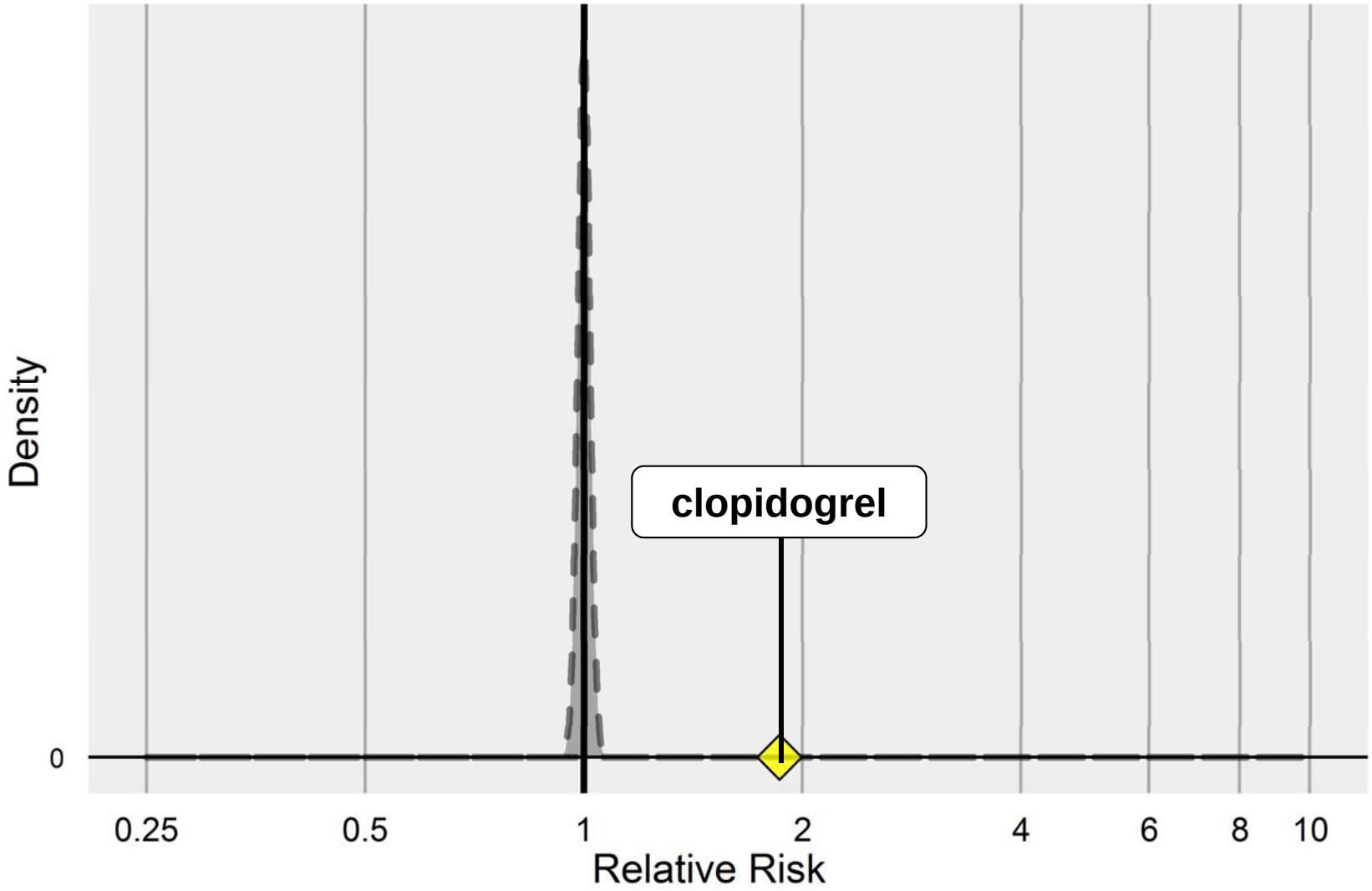
Negative Control for Null Hypothesis

	Positive controls	Negative controls	Total
Acute Liver Injury	81	37	118
Acute Myocardial Infarction	36	66	102
Acute Renal Failure	24	64	88
Upper Gastrointestinal Bleeding	24	67	91
Total	165	234	399

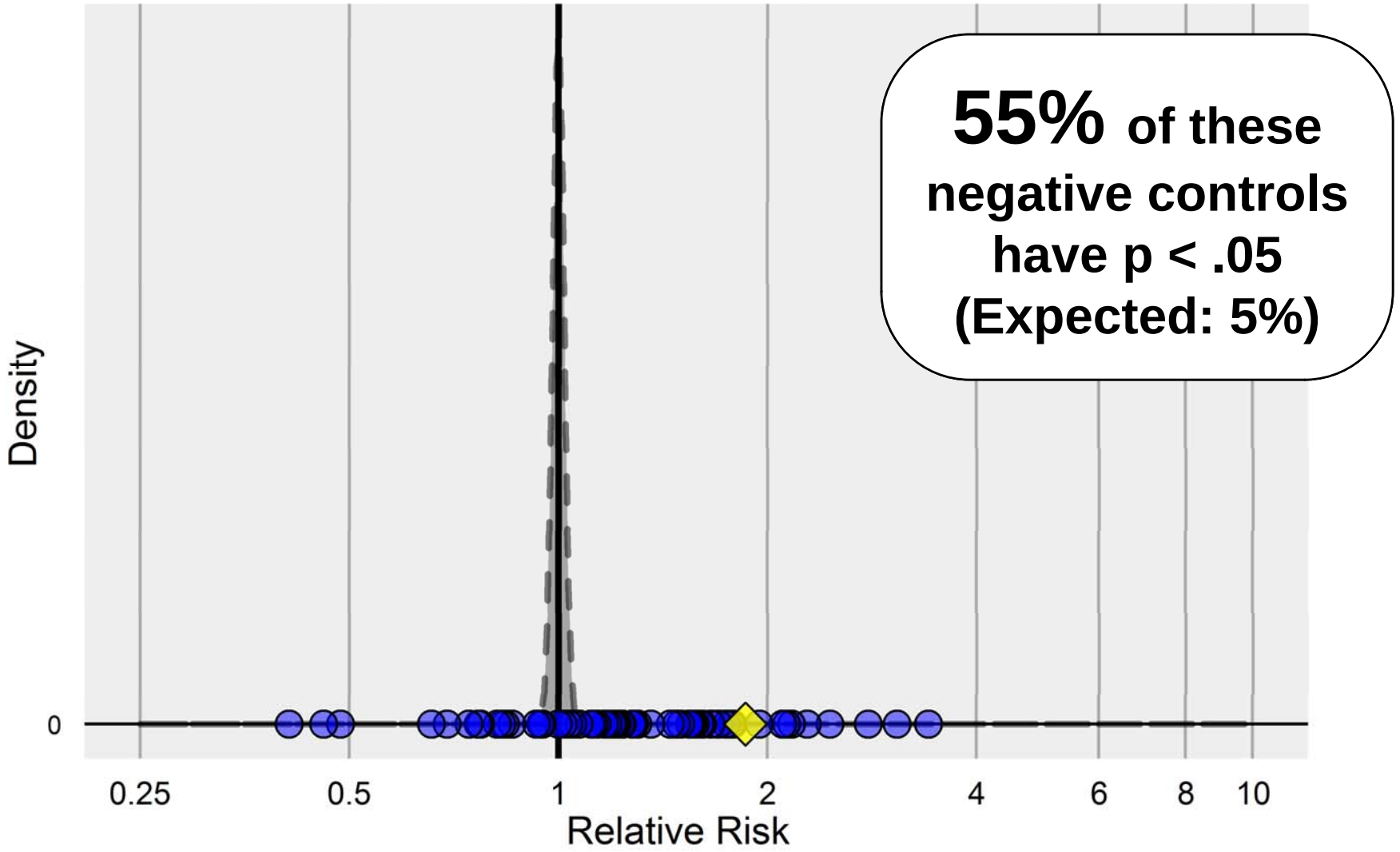
Criteria for negative controls:

- **Event not listed anywhere in any section of active FDA structured product label**
- **Drug not listed as 'causative agent' in Tisdale et al, 2010: "Drug-Induced Diseases"**
- **Literature review identified no evidence of potential positive association**

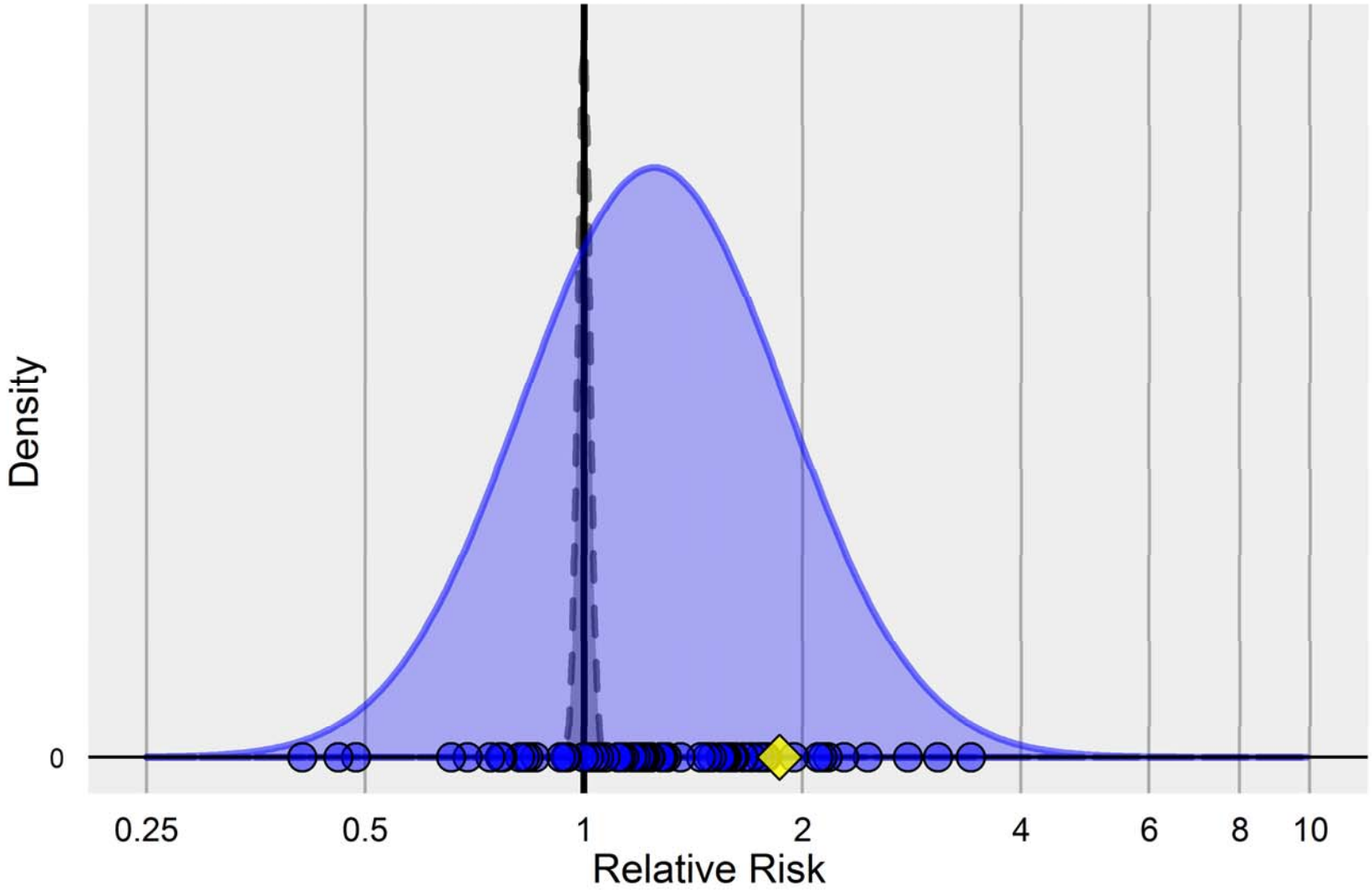
Negative controls & the null distribution



Negative controls & the null distribution



Negative controls & the null distribution



Assumption

For established drugs, we know the true effects

Metoprolol

Structured Product Label – Warnings and Precautions

- **METOPROLOL SUCCINATE- metoprolol succinate tablet, film coated, extended release**
  Wockhardt Limited

- Anaphylactic Reactions
- Bradycardia
- Bronchospastic Disease

- Diabetes and Hypoglycemia
- Heart Failure

- Ischemic Heart Disease
- Major Surgery

- Pheochromocytoma
- Thyrotoxicosis

- **TOPROL XL- metoprolol succinate tablet, extended release**
  AstraZeneca LP

- Anaphylactic Reactions

- Bronchospastic Disease
- Calcium Channel Blockers
- Diabetes and Hypoglycemia
- Heart Failure
- Hepatic Impairment
- Ischemic Heart Disease
- Major Surgery
- Peripheral Vascular Disease
  Pheochromocytoma
- Thyrotoxicosis

Assumption

We know how to handle data and analyses

We know how to do compliant research
Governance and Systems

Assumption: Data and Findings are regulated

• Quality of data	No record verification, no access to data generation
• Collection and submission of data	Data are publicly available
• Statistical Programming	Anemic systems for size of data
• Validation of systems	Impossible against unknown "predefined specs"

• Oversight committees
  • Whether or not
  • What data
  • What design
  • What parameter choices
	No parameters for right answer

Problems with RWE
Summary list

- Reproducibility problem
  - Effect estimates affected by choice of design and analysis parameters
- P-value calculations affected by bias
- No Gold Standards for outcome algorithms
- No Gold Standard for drug effects
- Data not collected for research, but "dirty" 2nd hand
- Inadequate Data Management and Compliance framework of clinical trial world

How do you want to do this right?

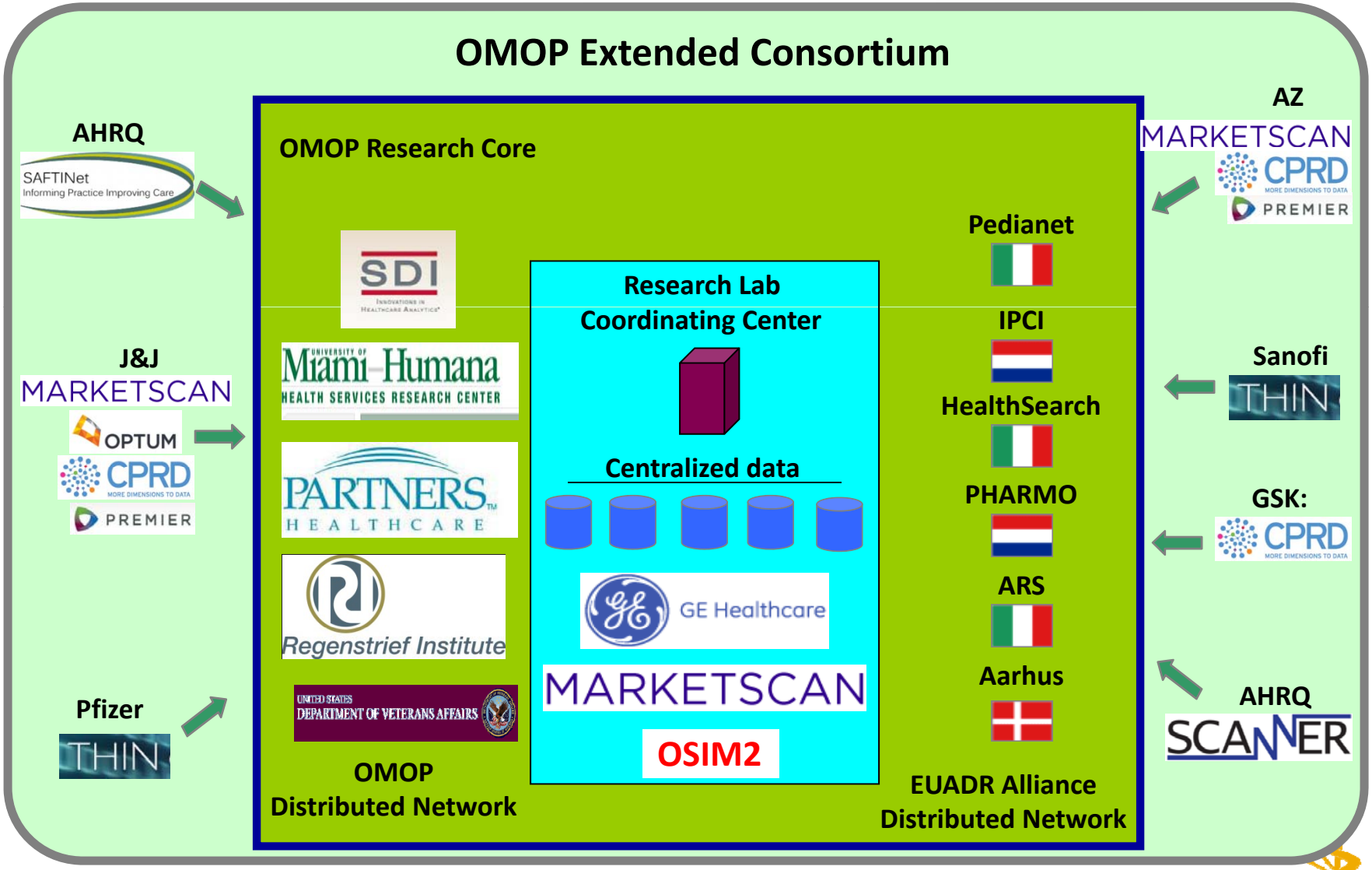
OMOP

OBSERVATIONAL
MEDICAL
OUTCOMES
PARTNERSHIP

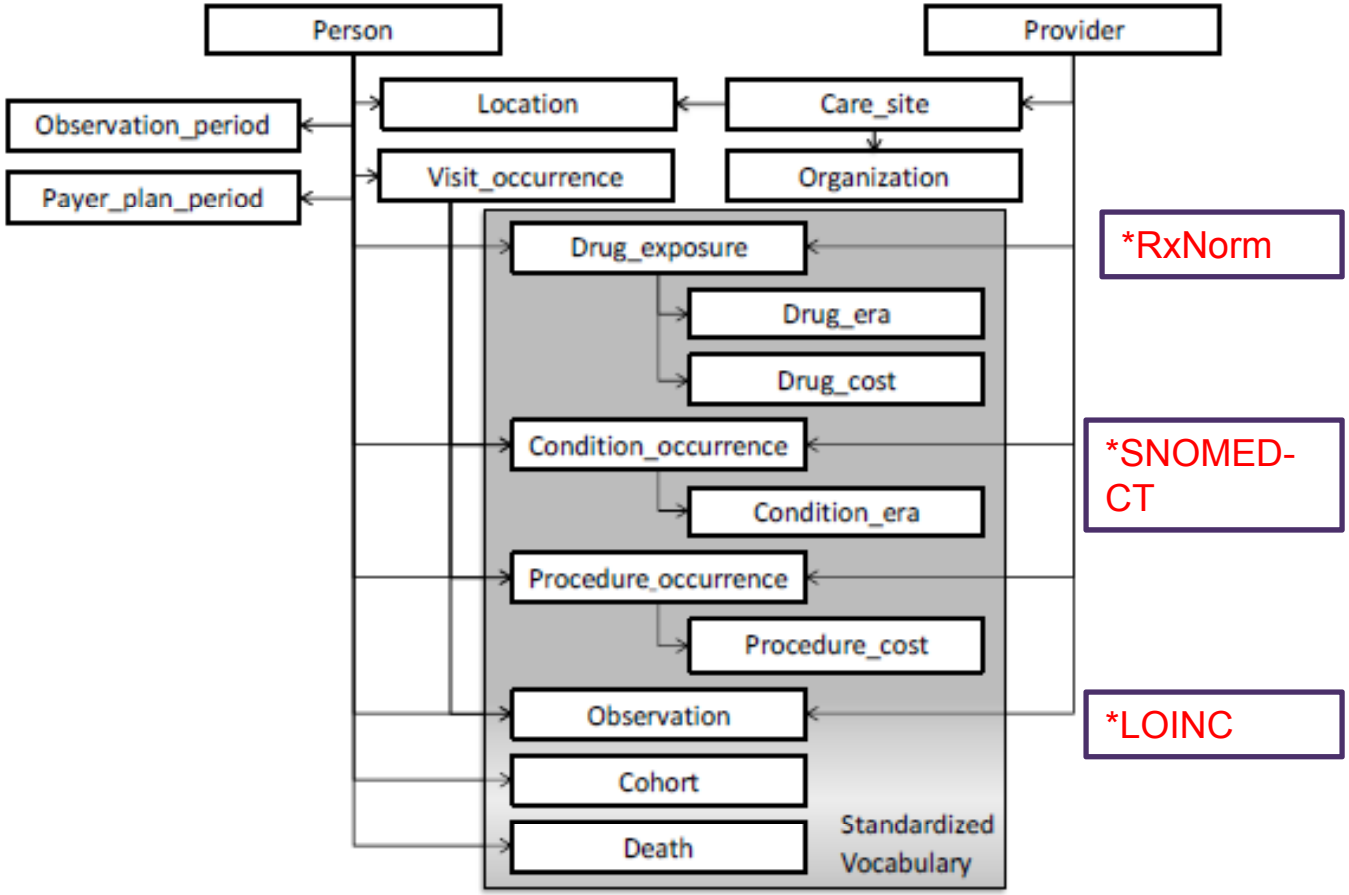
Standard Data Format
Standard Data Content (Coding)
Standard Data Characterization
Standard Methods
Systematic Research

Community
Vendor Ecosystem

OMOP Data Community



Standard Data Format



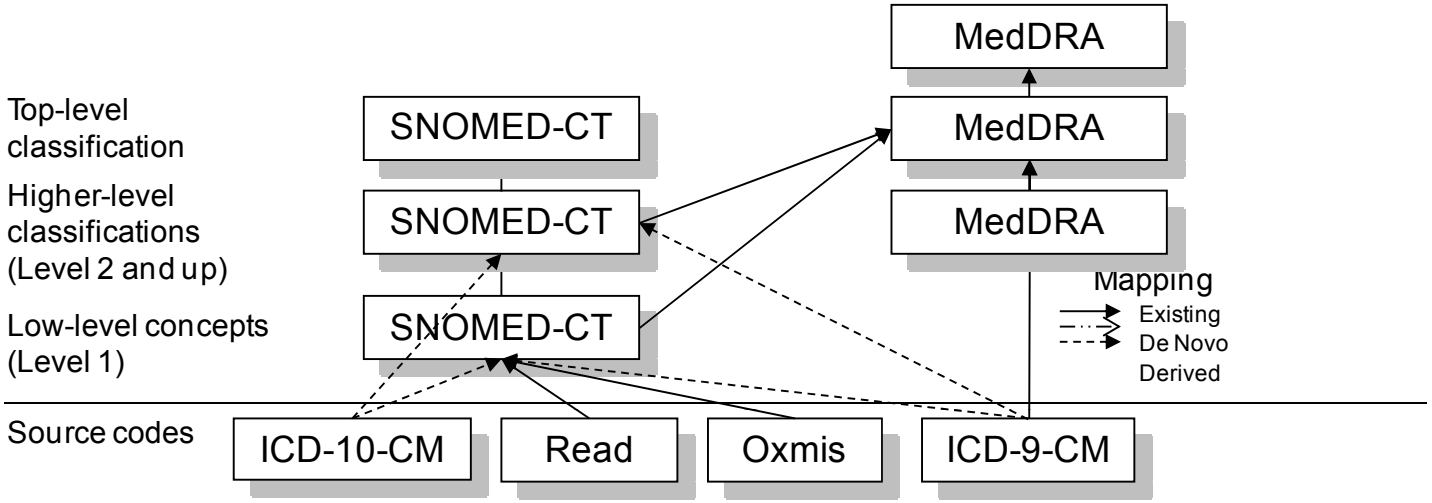
- Claims and EHRs
- Optimized for large-scale analytics
- Conceived for active medical product surveillance, but extensible for other use cases
- Applied successfully across OMOP data community

http://omop.fnih.org/CDMvocabV4

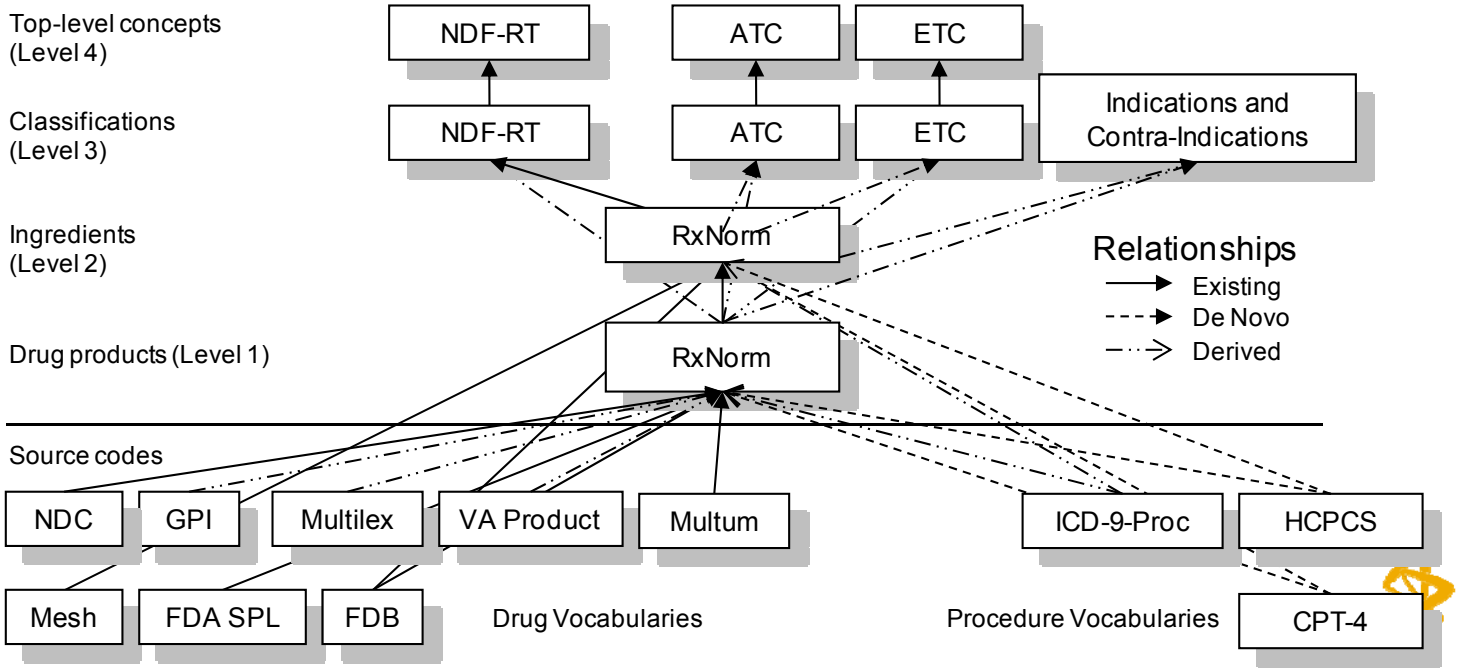
- Standards-based, conforming to ONC Meaningful Use Stage 2 recommendations

Standard Data Content

Standardizing conditions:

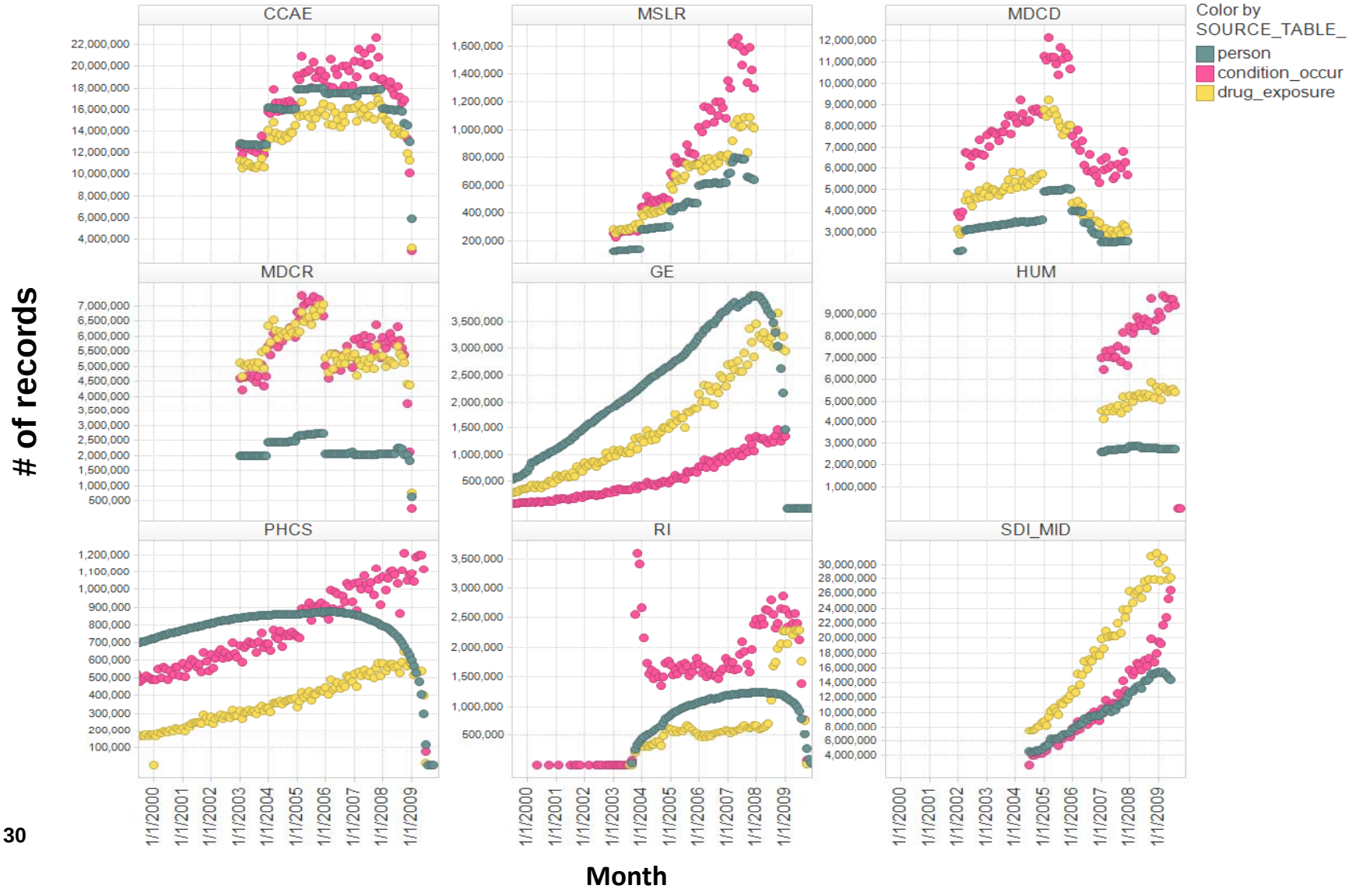


Standardizing drugs:

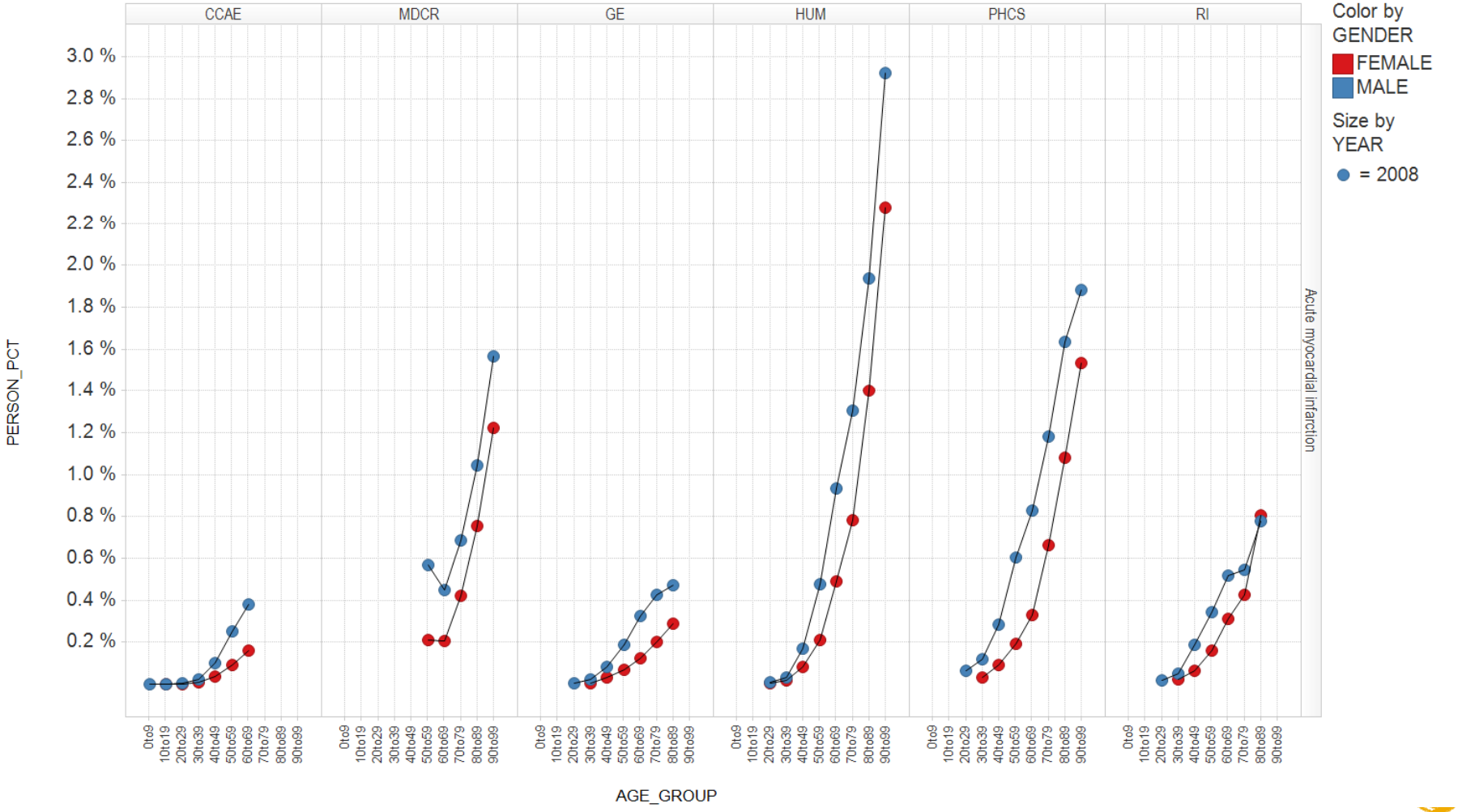


Standard Data Characteristics

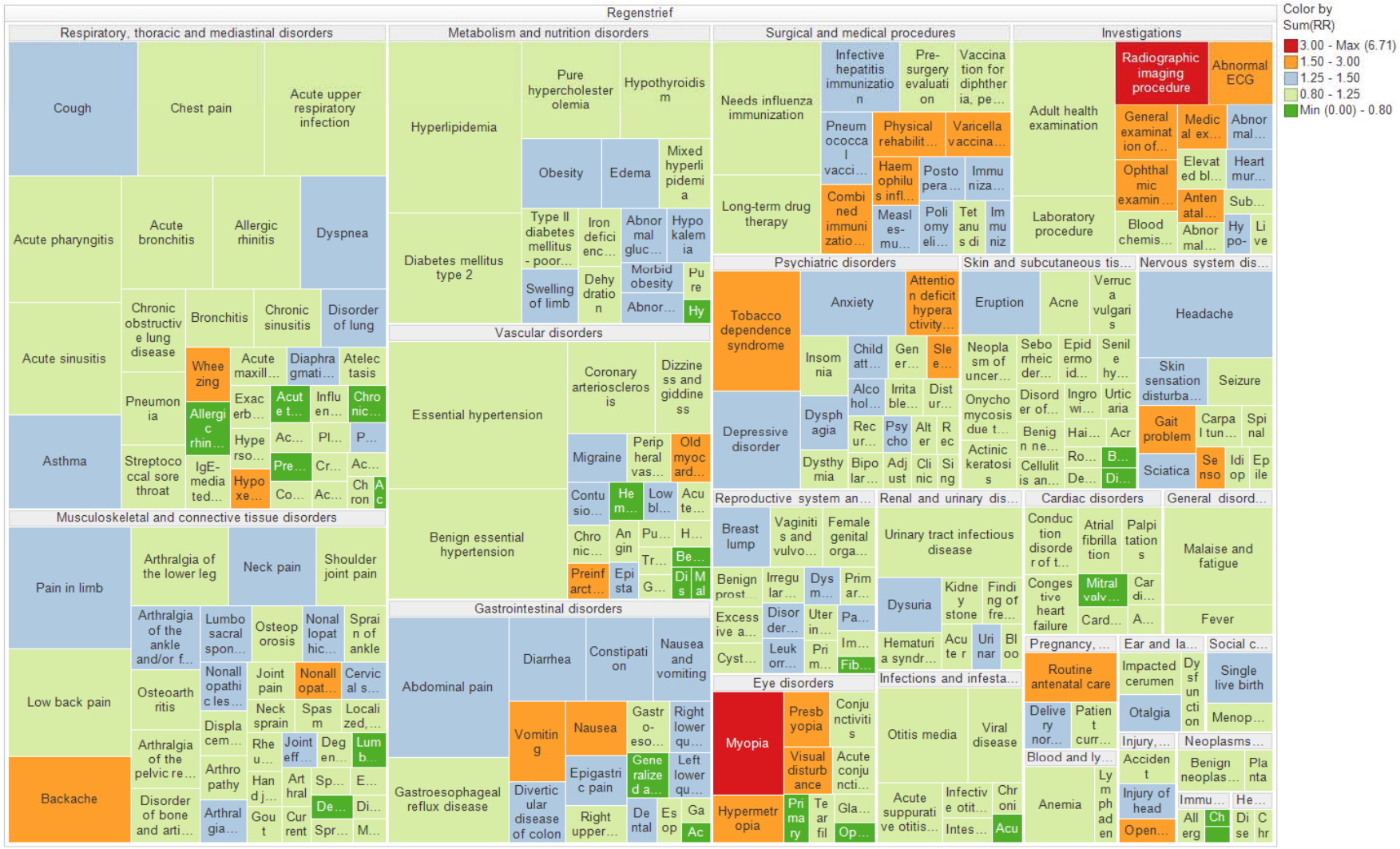
Records Over Time



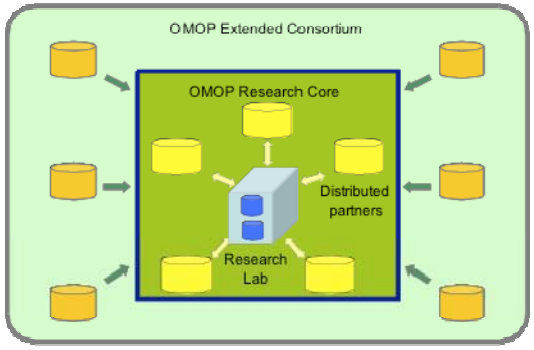
Standard Data Characteristics
Prevalence by Age and Gender



Standard Data Characteristics
Spotting Prevalence Differences

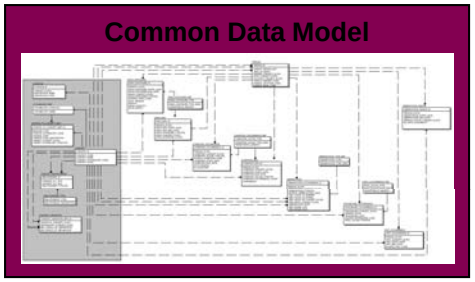


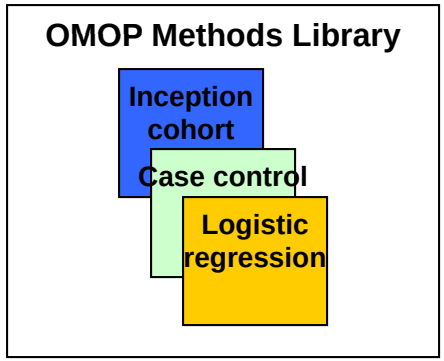
Systematic Evaluation with Test Cases



- 10 data sources
- Claims and EHRs
- 200M+ lives

- Open-source
- Standards-based





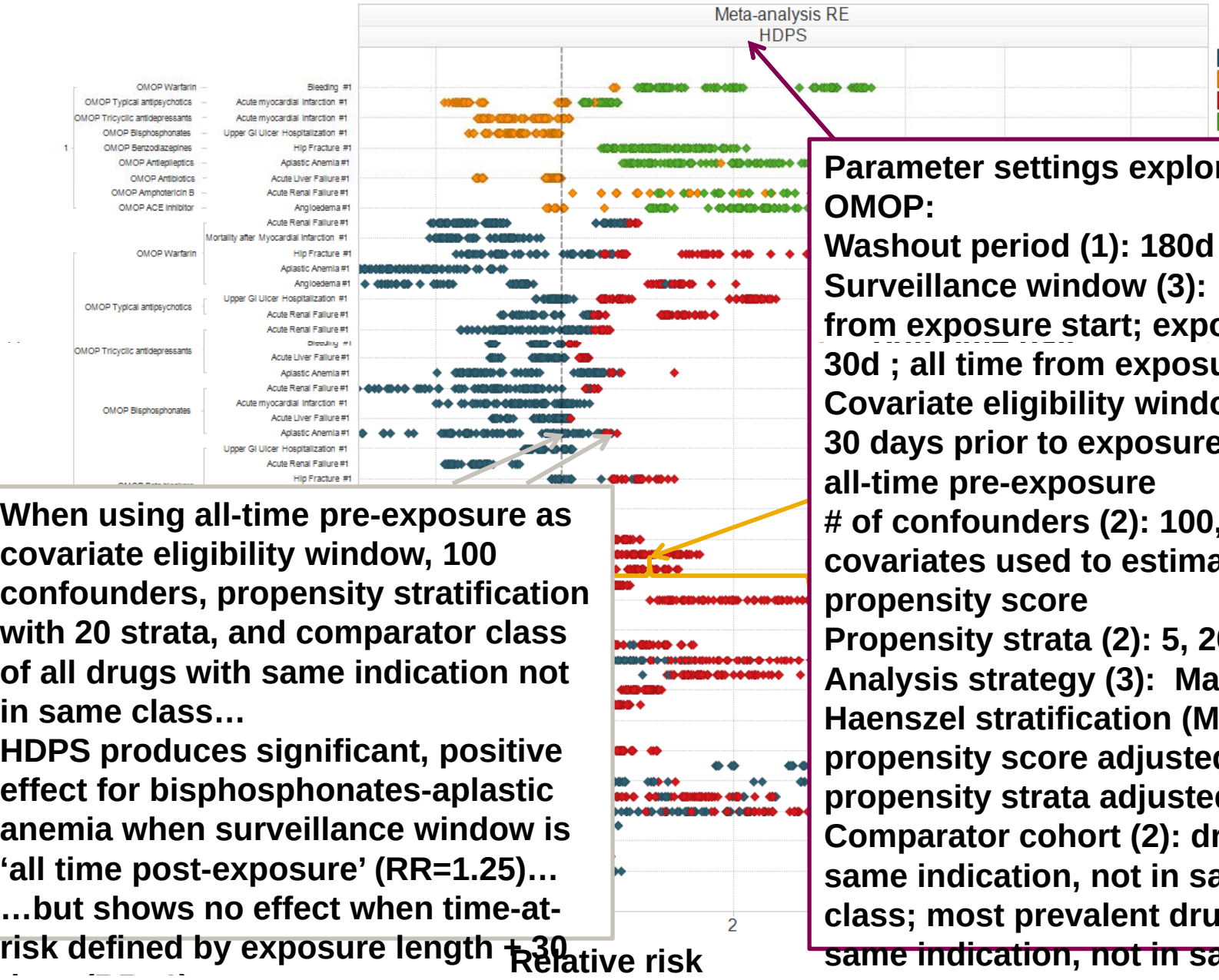
- 14 methods
- Epidemiology designs
- Statistical approaches adapted for longitudinal data

Drug

Outcome	ACE Inhibitors	Amphotericin B	Antibiotics: erythromycins, sulfonamides, tetracyclines	Antiepileptics: carbamazepine, phenytoin	Benzodiazepines	Beta blockers	Bisphosphonates: alendronate	Tricyclic antidepressants	Typical antipsychotics	Warfarin
Angioedema										
Aplastic Anemia										
Acute Liver Injury										
Bleeding										
Hip Fracture										
Hospitalization										
Myocardial Infarction										
Mortality after MI										
Renal Failure										
GI Ulcer Hospitalization										

Positives: 9
Negatives: 44

Systematic Evaluation of Methods



- When using all-time pre-exposure as covariate eligibility window, 100 confounders, propensity stratification with 20 strata, and comparator class of all drugs with same indication not in same class…
- HDPS produces significant, positive effect for bisphosphonates-aplastic anemia when surveillance window is 'all time post-exposure' (RR=1.25)…
- …but shows no effect when time-at-risk defined by exposure length + 30

Parameter settings explored in OMOP:

Washout period (1): 180d

Surveillance window (3): 30 days from exposure start; exposure + 30d ; all time from exposure start

Covariate eligibility window (3): 30 days prior to exposure, 180, all-time pre-exposure

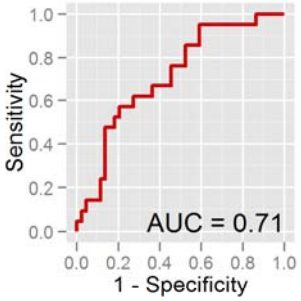
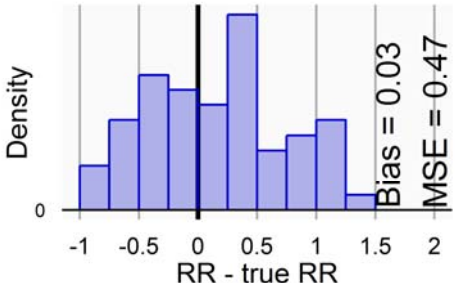
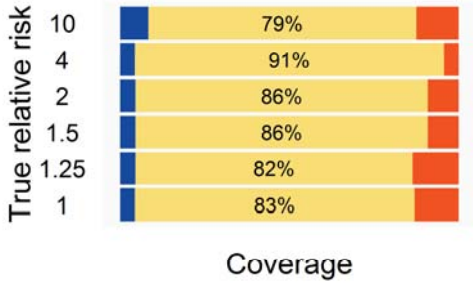
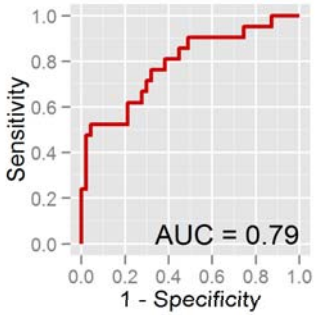
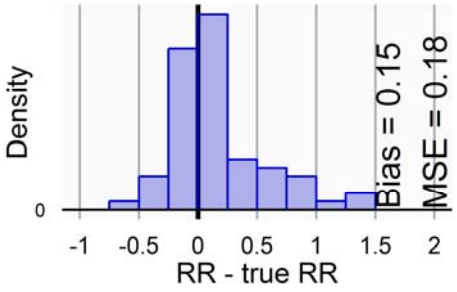
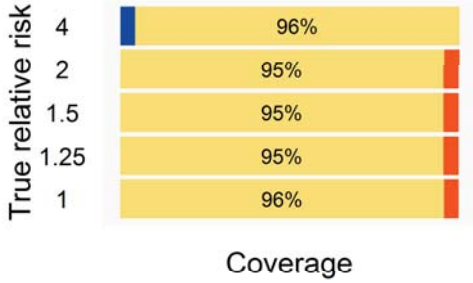
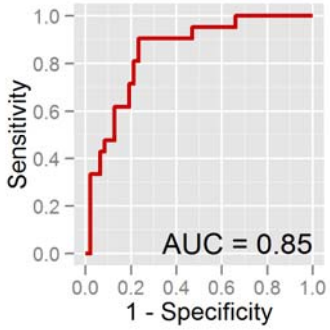
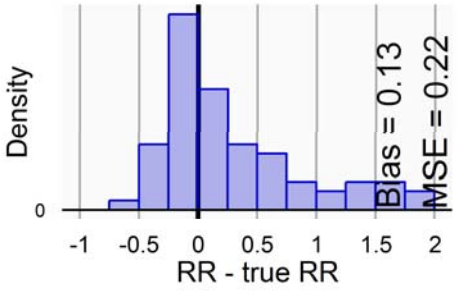
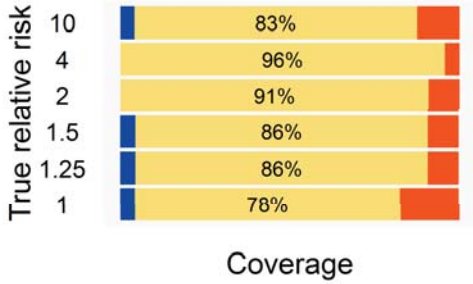
# of confounders (2): 100, 500 covariates used to estimate propensity score

Propensity strata (2): 5, 20 strata

Analysis strategy (3): Mantel-Haenszel stratification (MH), propensity score adjusted (PS), propensity strata adjusted (PS2)

Comparator cohort (2): drugs with same indication, not in same class; most prevalent drug with same indication, not in same

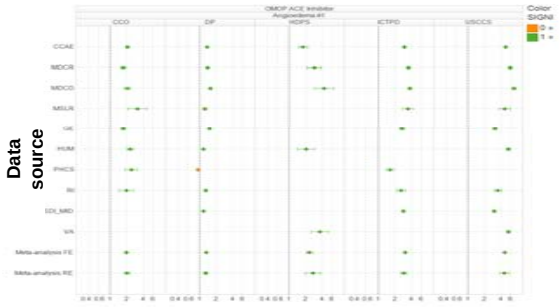
Comparing accuracy of cohort and self-controlled designs, after empirical calibration

	Discrimination	Error	Coverage	
CM: 21000214 **New user cohort, propensity score stratification, with active comparator (drugs known to be negative controls for outcome)**				**Bias: -0.02** **MSE: 0.38** **Mean SE: 0.36**
SCCS: 1955010 **Multivariate self-controlled case series, including all events, and defining time-at-risk as all-time post-exposure**				**Bias: 0.04** **MSE: 0.33** **Mean SE: 0.67**
OS: 403002 **Self-controlled cohort design, including all exposures and outcomes, defining time-at-risk and control time as length of exposure +**				**Bias: 0.00** **MSE: 0.11** **Mean SE: 0.25**

Vision for a risk identification and analysis system ‘causal dashboard’

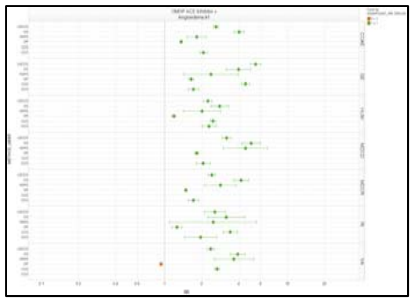
Drug ACE inhibitors ▼ **Outcome** Angioedema ▼

Strength of association

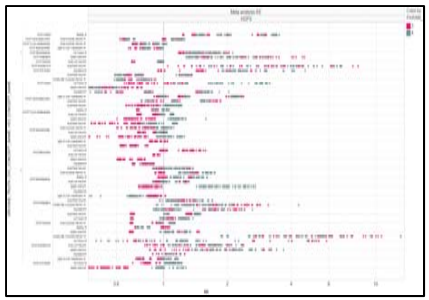


Consistency

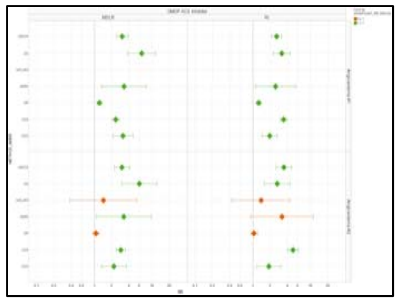
by data source



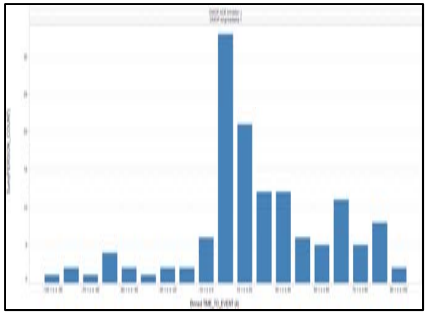
by method and parameters



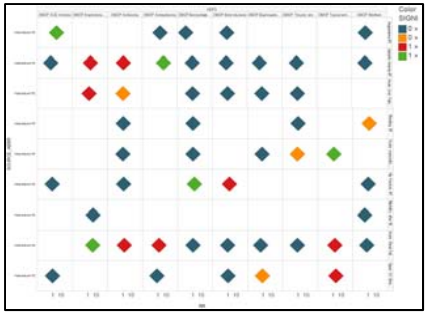
by outcome definition



Temporality

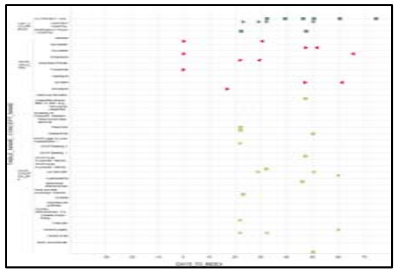


Specificity

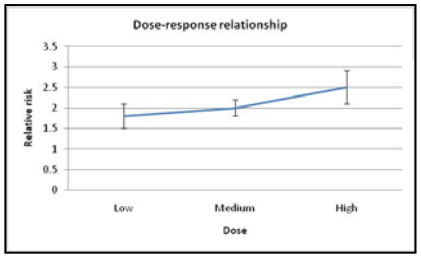


Plausibility

Interactive patient profiles



Biological gradient

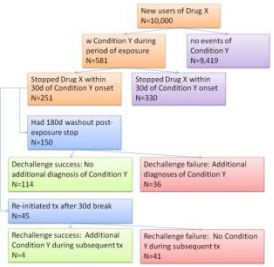


Analogy

Explore related conditions and treatments

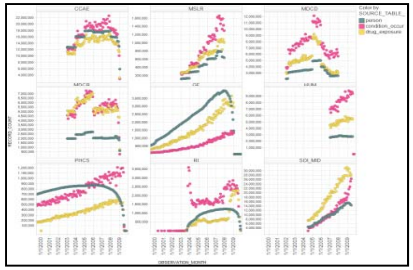
Experimental evidence

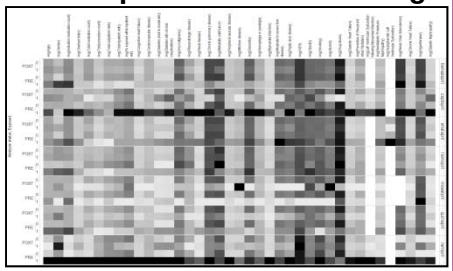
Dechallenge/Rechallenge



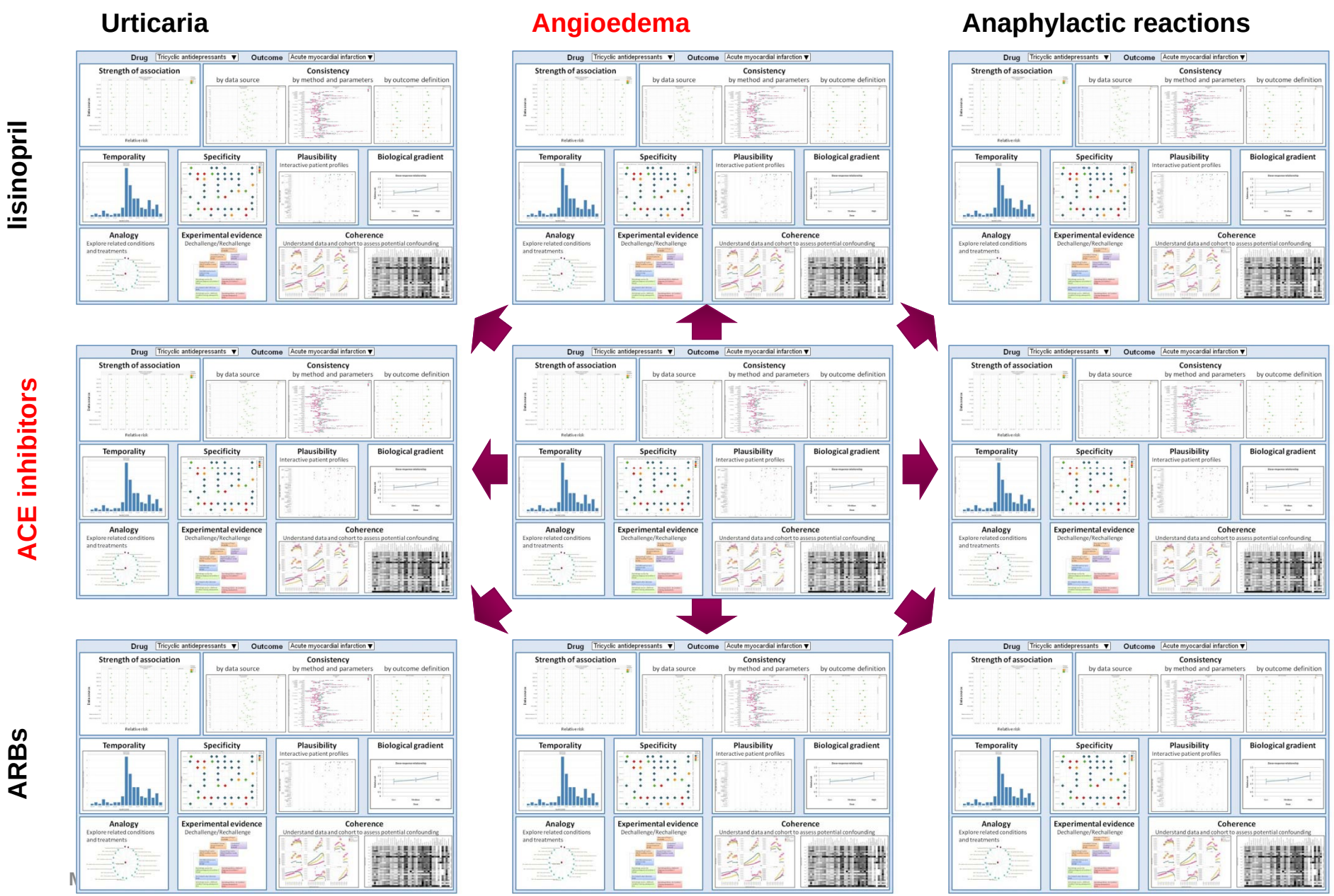
Coherence

Understand data and cohort to assess potential confounding





Systematic Exploratory Framework for studying effects



Summary

What RWE Research do we need?

- Systematic
  - Common data model
  - Empirical evaluation of solutions
  - Creations and sharing of Gold Standards
- Fully transparent
  - Open source methods
  - No restrictions on scientific questions ("afraid how the public could interpret the finding")
- Interdisciplinary
  - Industry
  - Academics
  - Government
- OMOP provides a platform
  - Standardization, community, ecosystem
  - Systematic analysis
  - Ability to compare across data sources

Come to the OMOP-IMEDS Symposium 2013

November 5 – 6, 2013
Hyatt Regency Bethesda