

SIGNAL DETECTION IN  
OBSERVATIONAL DATABASES: DOES  
ANYONE KNOW IF IT WORKS?

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# NOBODY KNOWS



[dreamstime.com](http://dreamstime.com)

BUT WE ARE GETTING THERE...



IT WILL NEITHER “WORK”  
NOR “NOT WORK”

Need to characterize how  
well does it work

“Operating Characteristics”

Diagnostic Analogy: Home  
Pregnancy Test



IDEALLY...



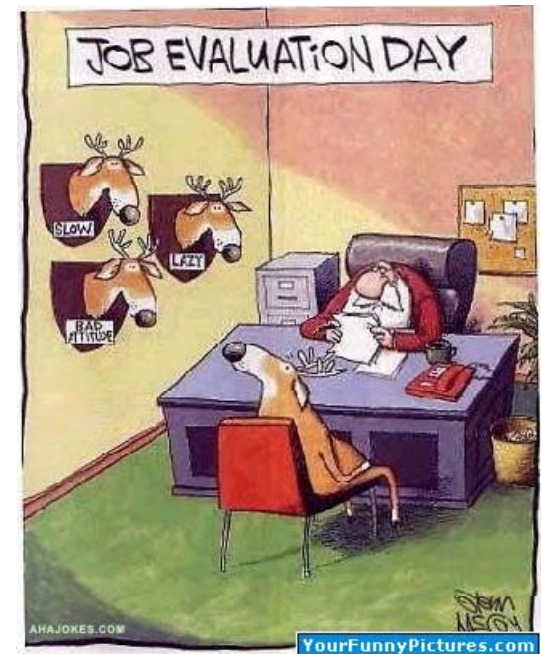
**Collection of drug-outcome pairs  
with known relative risk**

**Empirically evaluate how close  
different method-database  
combinations get to the true  
relative risk (e.g., mean square  
error)**

## AN APPROACH...

**Have a collection of drug-outcome pairs with known causal status (yes/no)**

**Empirically evaluate how well different method-database combinations discriminate between the yes's and no's**

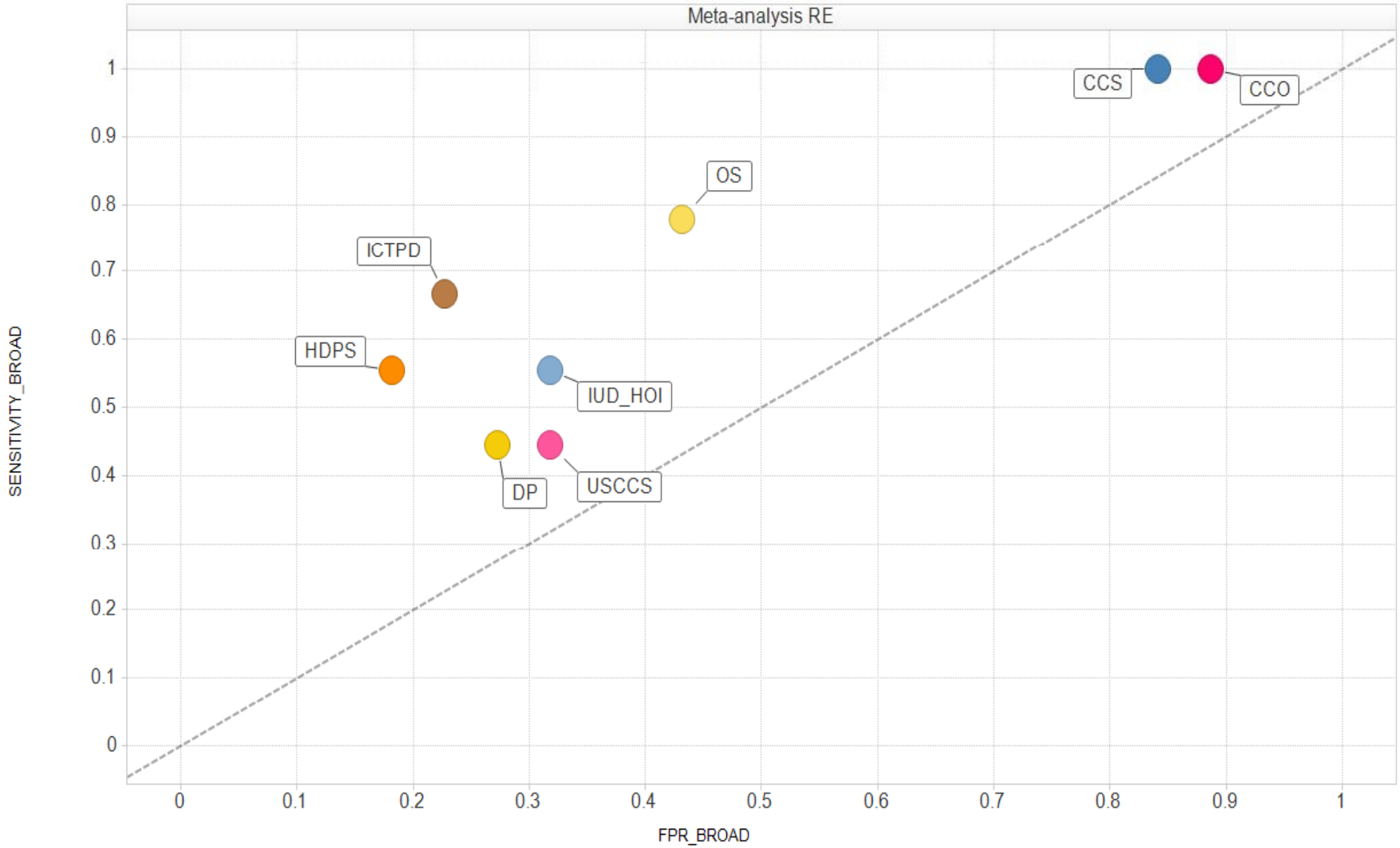


# THE OMOP EXPERIMENT

Outcome	ACE Inhibitors	Amphotericin B	Antibiotics: erythromyoin, sulfonamides, tetracyclines	Anti epile ptics: carbamazepine, phenytoin	Benzodiazepines	Beta blockers	Bisphosphonates: alendronate	Tricyclic antidepressants	Typical antipsychotics	Warfarin
Angioedema	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Aplastic Anemia	Negative control'	Negative control'	Negative control'	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Acute Liver Injury	Negative control'	Negative control'	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Bleeding	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	True positive' risk	Negative control'	True positive' risk
Hip Fracture	Negative control'	Negative control'	Negative control'	Negative control'	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Hospitalization	True positive' benefit	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Myocardial Infarction	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	True positive' risk	True positive' risk	Negative control'	Negative control'
Mortality after MI	Negative control'	Negative control'	Negative control'	Negative control'	True positive' benefit	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
Renal Failure	Negative control'	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'
GI Ulcer Hospitalization	Negative control'	Negative control'	Negative control'	Negative control'	Negative control'	True positive' risk	Negative control'	Negative control'	Negative control'	Negative control'

Legend	Total
True positive' benefit	2
True positive' risk	9
Negative control'	44

Meta-analysis RE



# MANY LIMITATIONS

**Only 53 pairs**

**Older drugs**

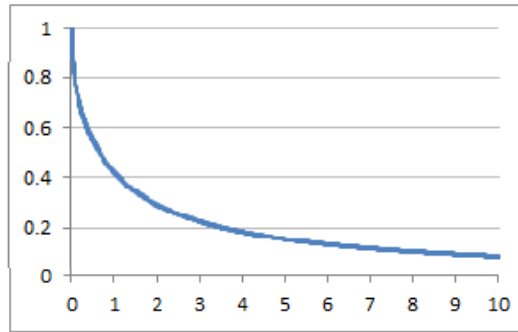
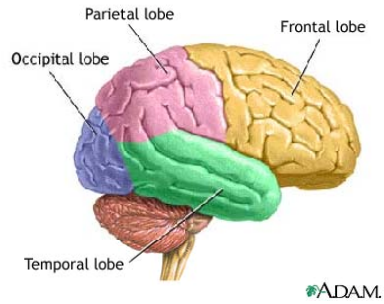
**Only 10 health outcomes of interest**

**Specific choice of parameters for each method**

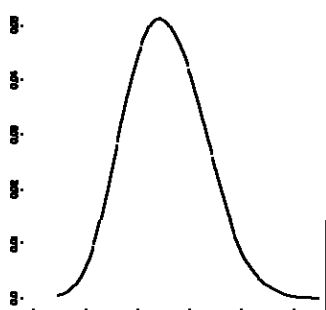
**Time to detection?**



# BAYESIAN LEARNING PARADIGM



prior

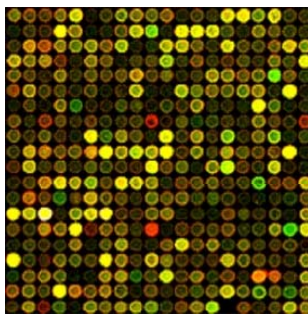


prior

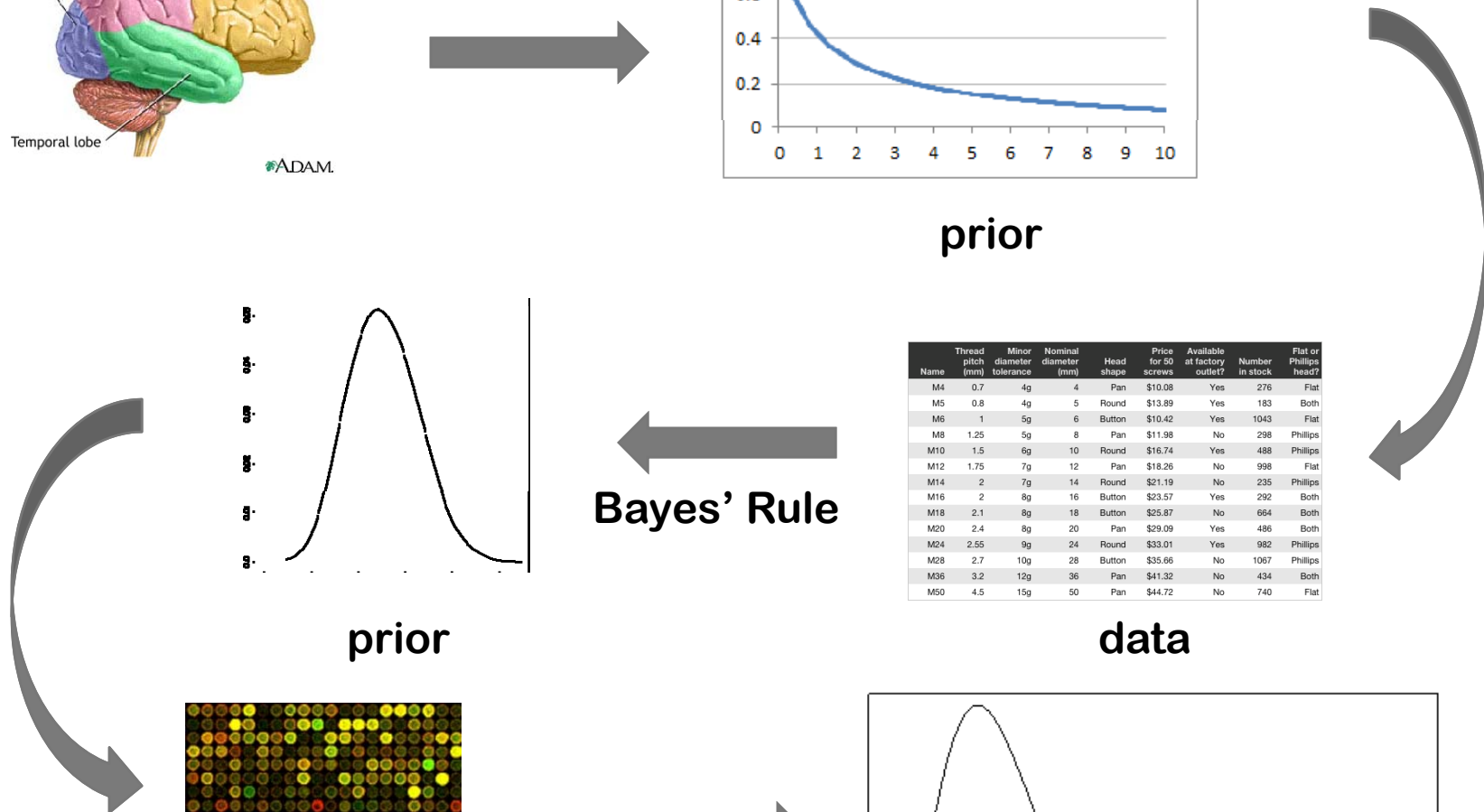
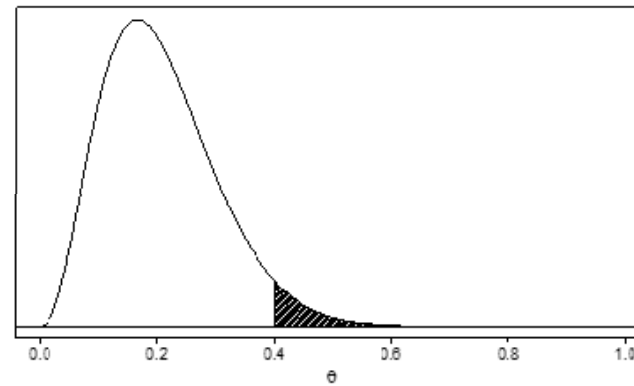
Bayes' Rule

Name	Thread pitch (mm)	Minor diameter tolerance	Nominal diameter (mm)	Head shape	Price for 50 screws	Available at factory outlet?	Number in stock	Flat or Phillips head?
M4	0.7	4g	4	Pan	\$10.08	Yes	276	Flat
M5	0.8	4g	5	Round	\$13.89	Yes	183	Both
M6	1	5g	6	Button	\$10.42	Yes	1043	Flat
M8	1.25	5g	8	Pan	\$11.98	No	298	Phillips
M10	1.5	6g	10	Round	\$16.74	Yes	488	Phillips
M12	1.75	7g	12	Pan	\$18.26	No	998	Flat
M14	2	7g	14	Round	\$21.19	No	235	Phillips
M16	2	8g	16	Button	\$23.57	Yes	292	Both
M18	2.1	8g	18	Button	\$25.87	No	664	Both
M20	2.4	8g	20	Pan	\$29.09	Yes	486	Both
M24	2.55	9g	24	Round	\$33.01	Yes	982	Phillips
M28	2.7	10g	28	Button	\$35.66	No	1067	Phillips
M36	3.2	12g	36	Pan	\$41.32	No	434	Both
M50	4.5	15g	50	Pan	\$44.72	No	740	Flat

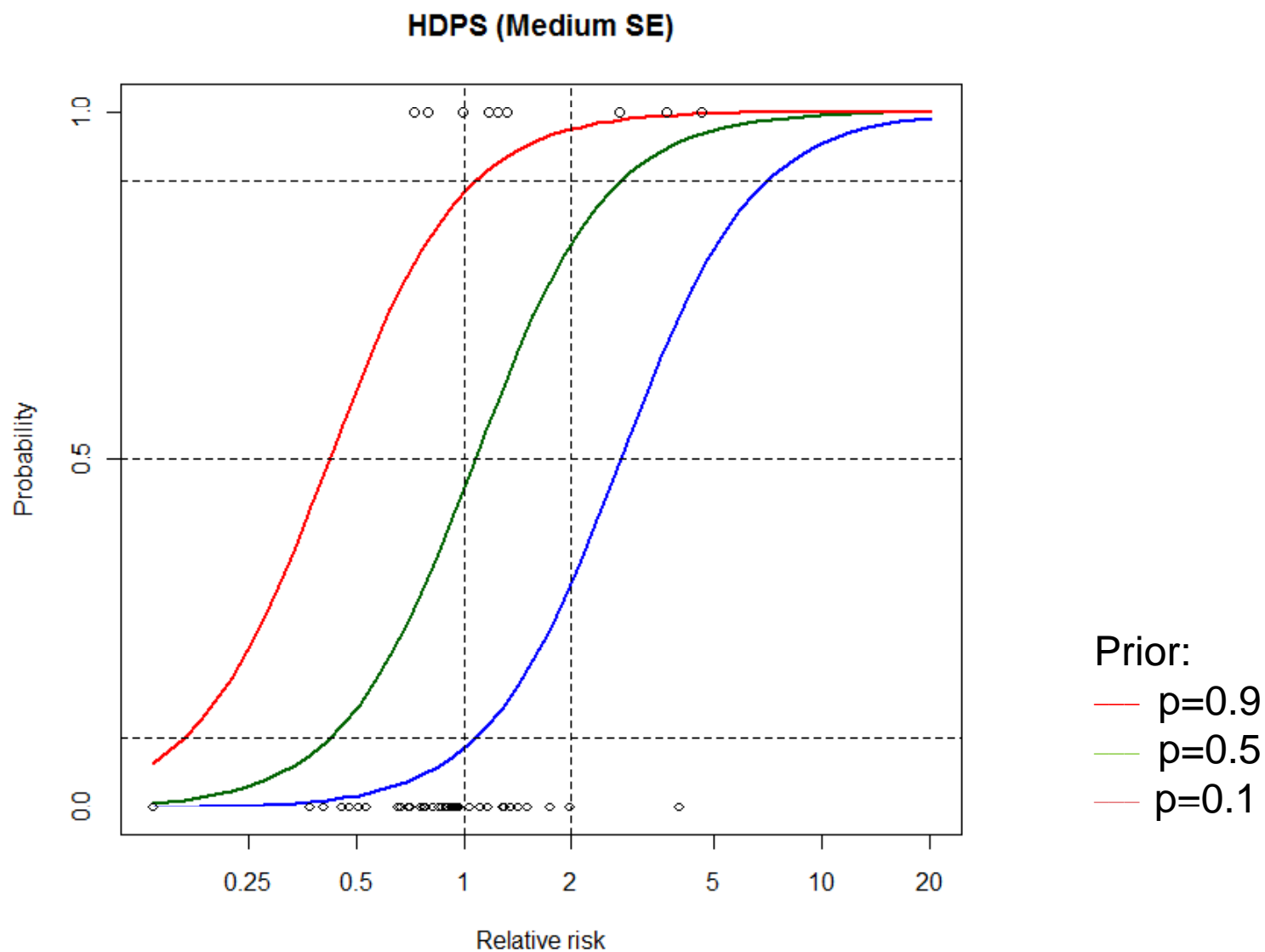
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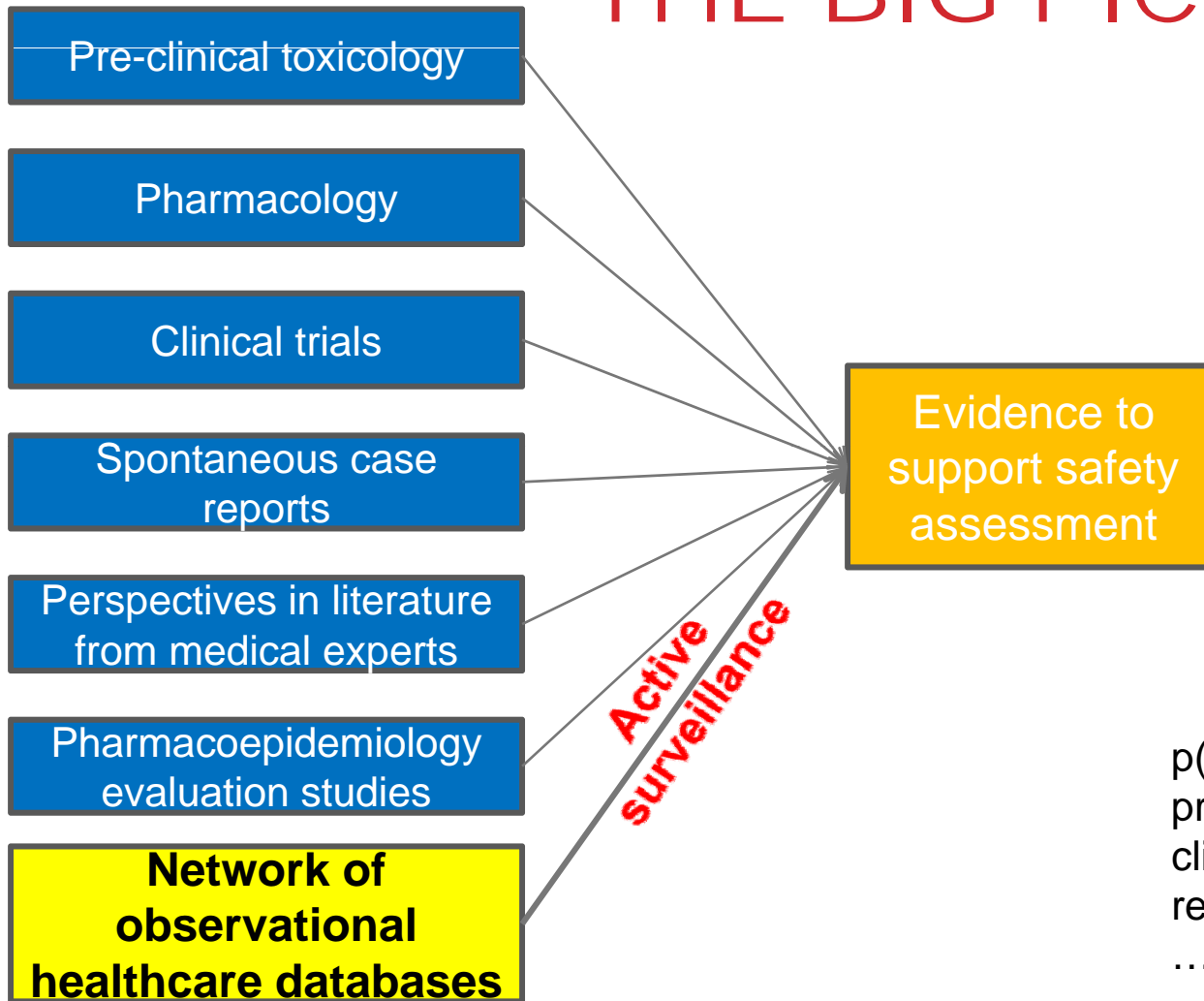
data



# HERE'S WHAT WE LEARN FROM THE OMOP EXPERIMENT

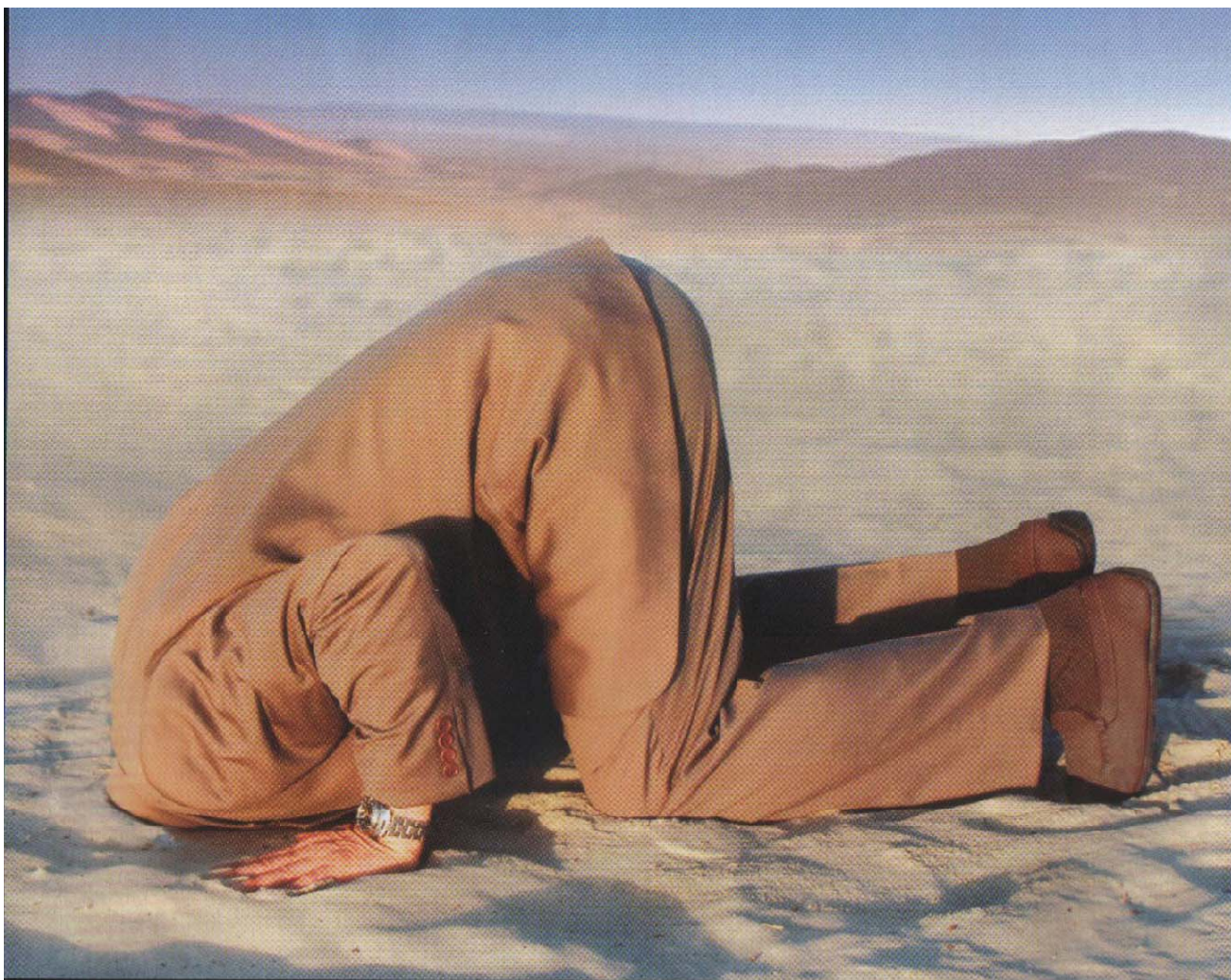


# THE BIG PICTURE



$p(\text{true unfavorable effect} \mid \text{pre-clinical, pharmacology, clinical trials, spontaneous reports, observational data, ...})$

LET'S NOT DO THIS!



# CONCLUSIONS

**Observational healthcare data can be used to efficiently generate evidence about the potential effects of medical products**

**The confidence in that evidence needs to be based on the operating characteristics of observational analyses**

**The risk identification and analysis system will be only one piece of information that needs to be integrated with all other existing evidence to provide a more comprehensive safety assessment**

**Safety assessments always need to be put into broader context with evidence about benefits and alternative treatments, incorporating stakeholder perspectives to guide medical decision-making**