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

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NOBODY KNOWS

BUT WE ARE GETTING THERE…

IT WILL NEITHER "WORK" NOR "NOT WORK"

Need to characterize how *well* does it work

"Operating Characteristics"

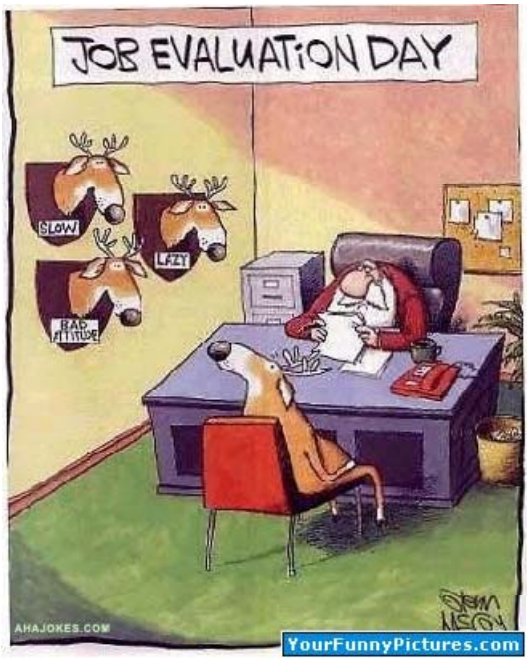
Diagnostic Analogy: Home Pregnancy Test

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)

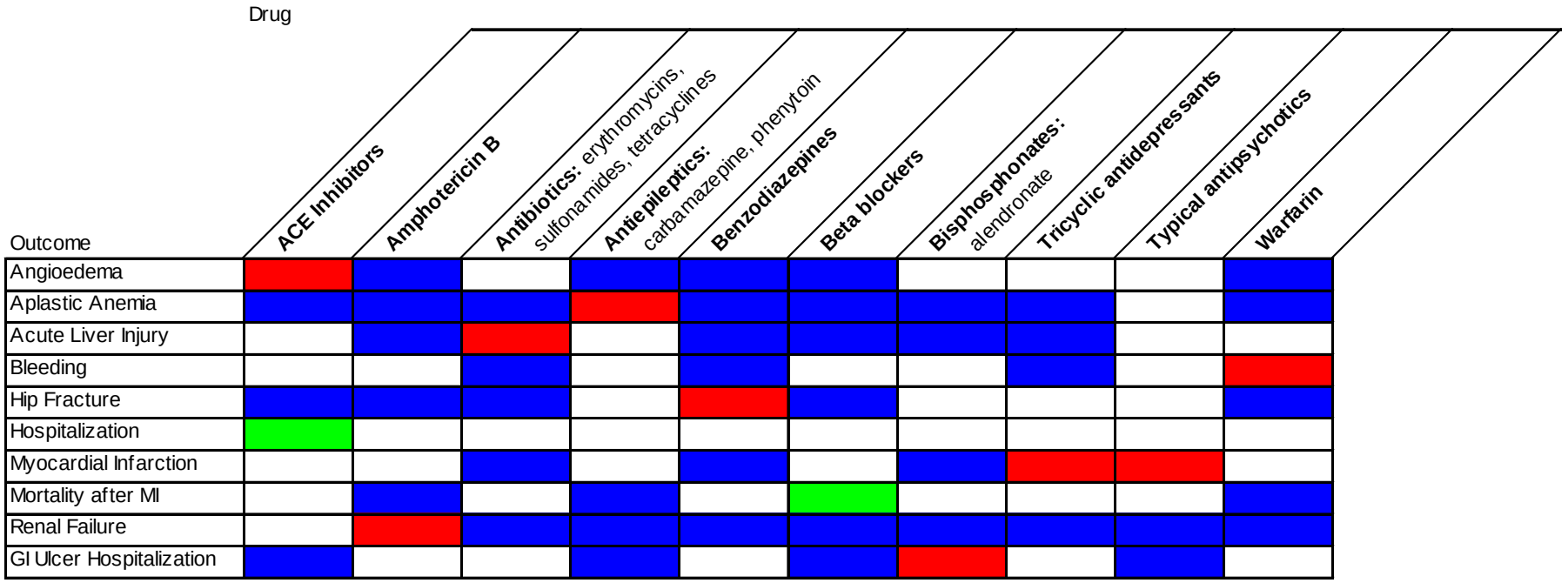
AN APPROACH...



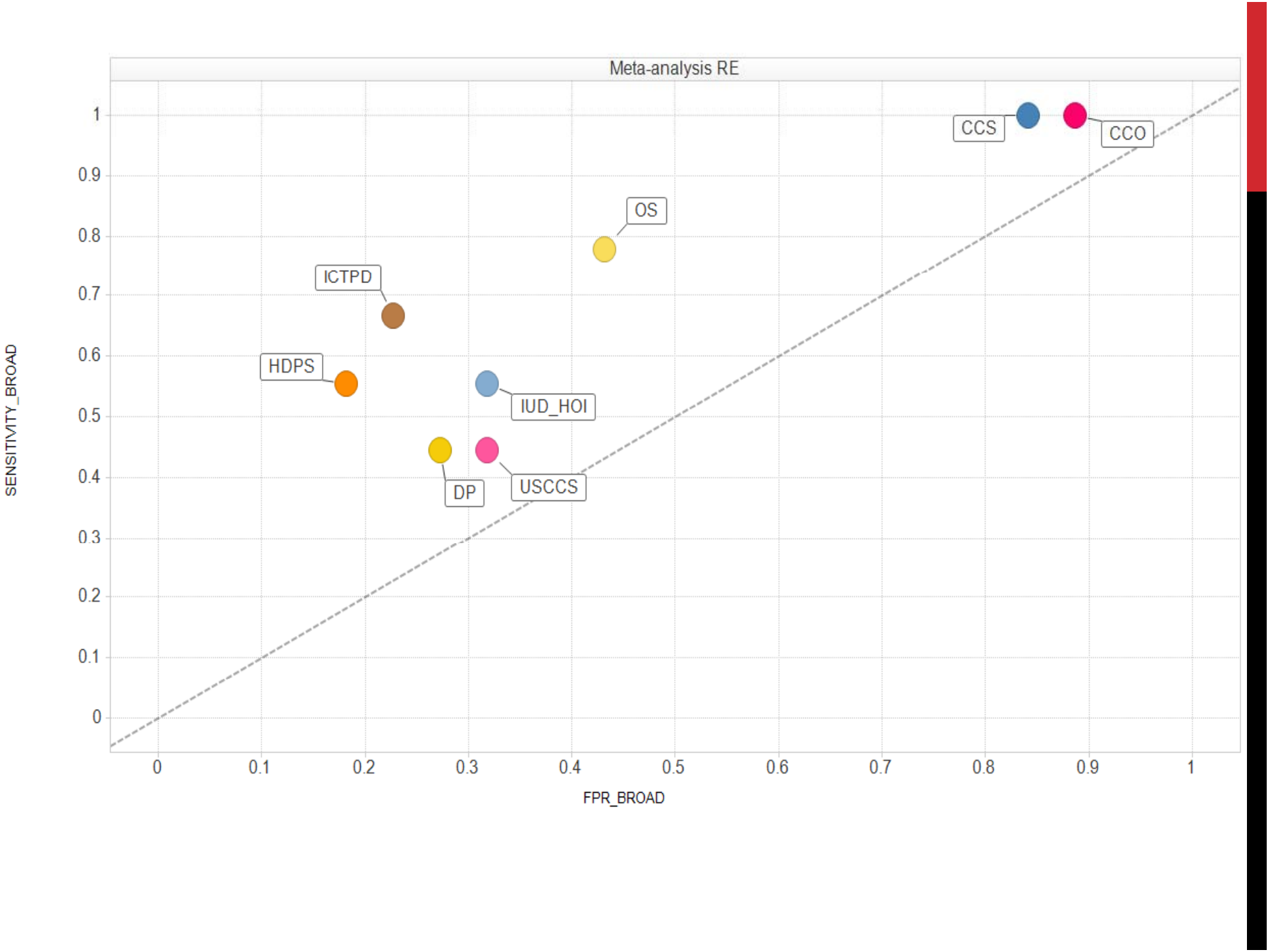
Have a collection of drug-outcome pairs with known causal status (yes/no)

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

THE OMOP EXPERIMENT



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


Meta-analysis RE
SENSITIVITY_BROAD
FPR_BROAD
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
CCS
CCO
OS
ICTPD
HDPS
IUD_HOI
DP
USCCS

MANY LIMITATIONS

Only 53 pairs

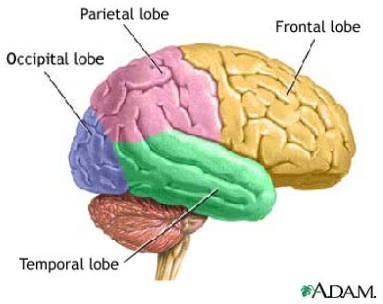
Older drugs

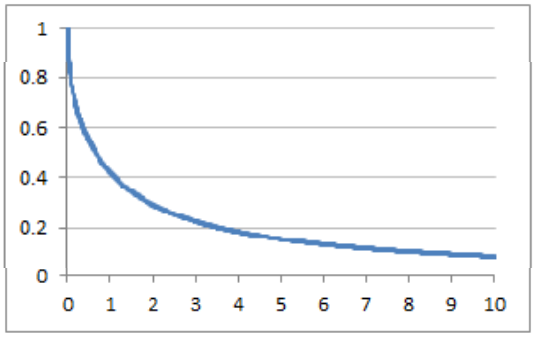
Only 10 health outcomes of interest

Specific choice of parameters for each method

Time to detection?

BAYESIAN LEARNING PARADIGM



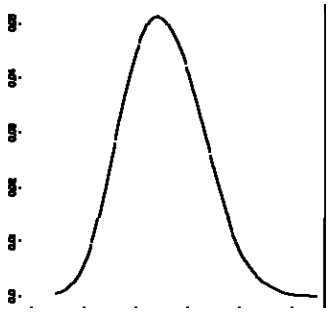


prior

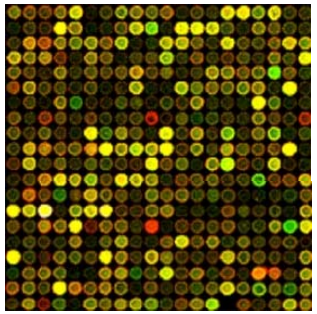
Name	Thread pitch (mm)	Minor diameter tolerance	Nominal diameter (mm)	Head shape	Price for 50 screws	Available at factory outlet?	Number in stock	Flat or Phillips head?
M4	0.7	4g	4	Pan	$10.08	Yes	276	Flat
M5	0.8	4g	5	Round	$13.89	Yes	183	Both
M6	1	5g	6	Button	$10.42	Yes	1043	Flat
M8	1.25	5g	8	Pan	$11.98	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

data

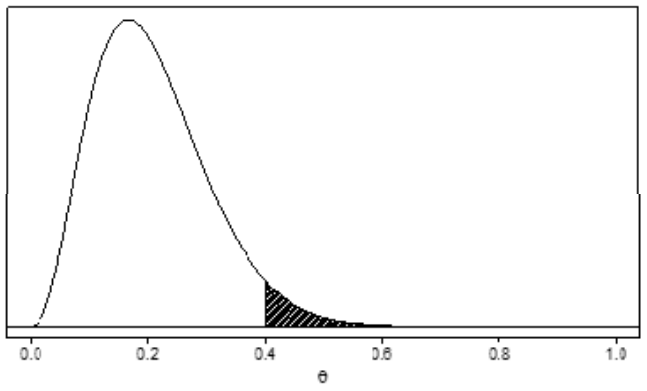
Bayes' Rule



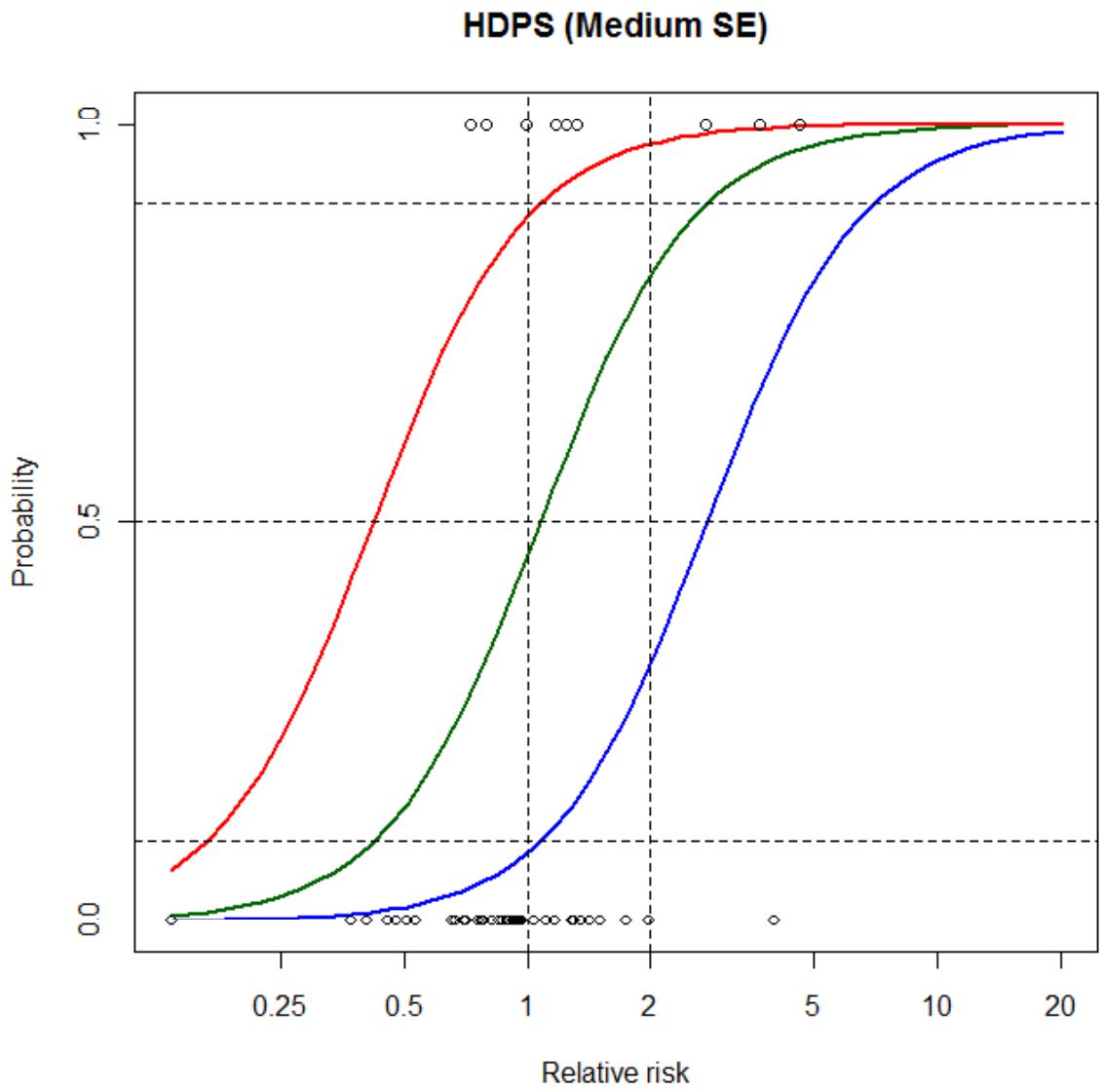
prior



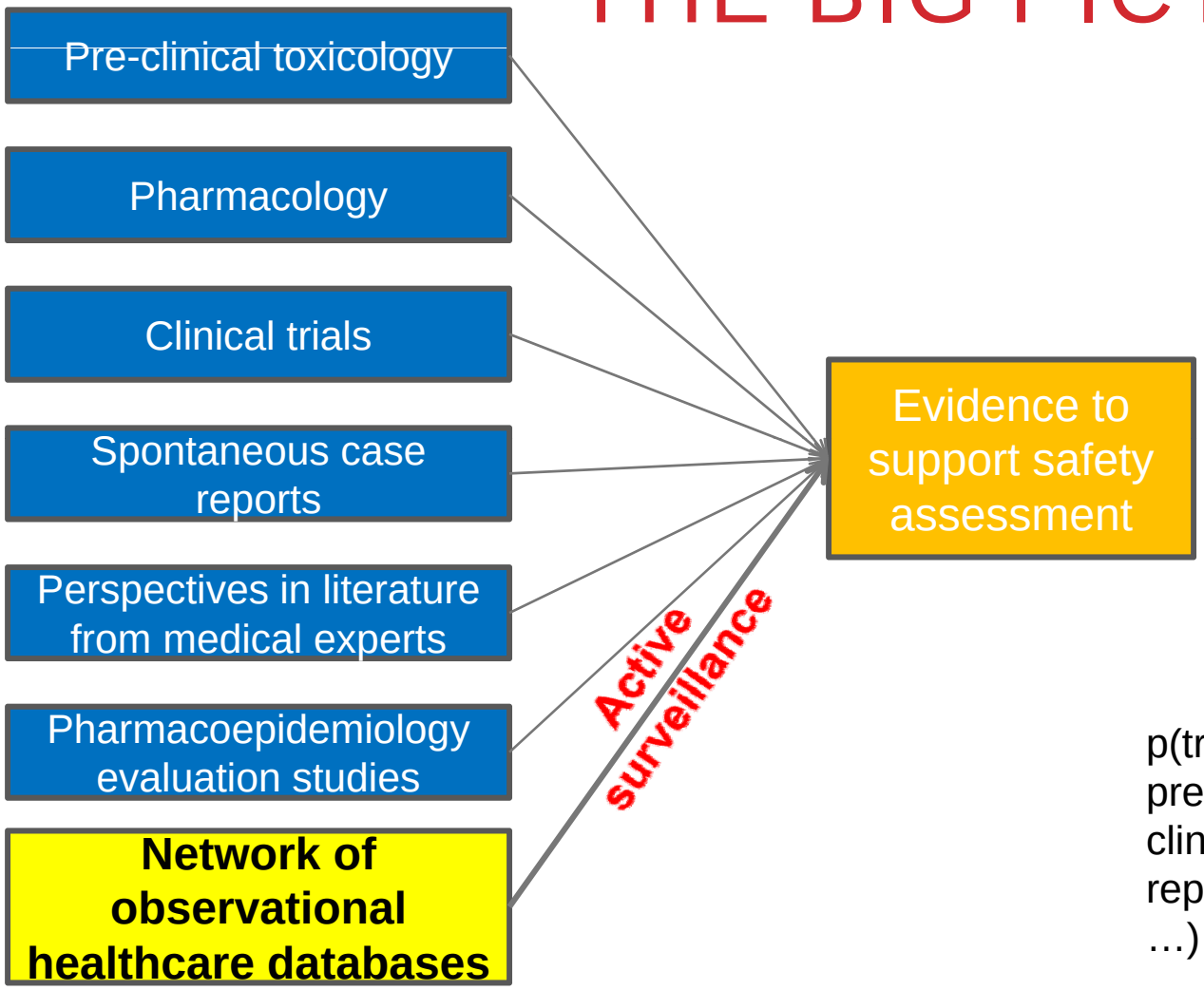
data



HERE'S WHAT WE LEARN FROM THE OMOP EXPERIMENT



THE BIG PICTURE



p(true **unfavorable** effect | 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 be to 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