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Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium

Pre-symposium training: Introduction to disproportionality analysis

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NOVARTIS

PROTECT Symposium February 19-20 2015

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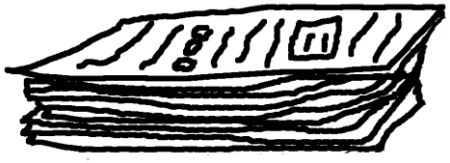

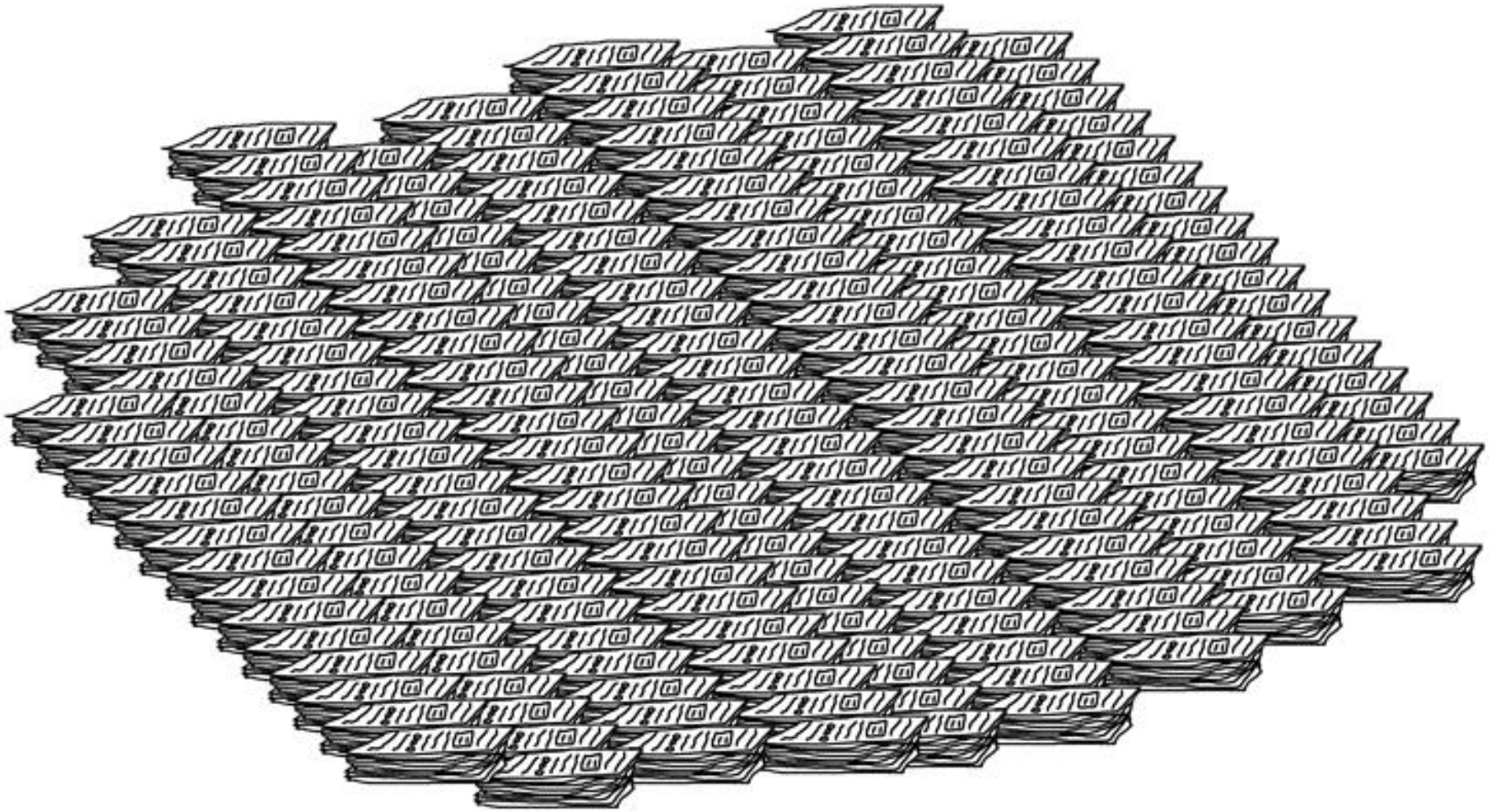

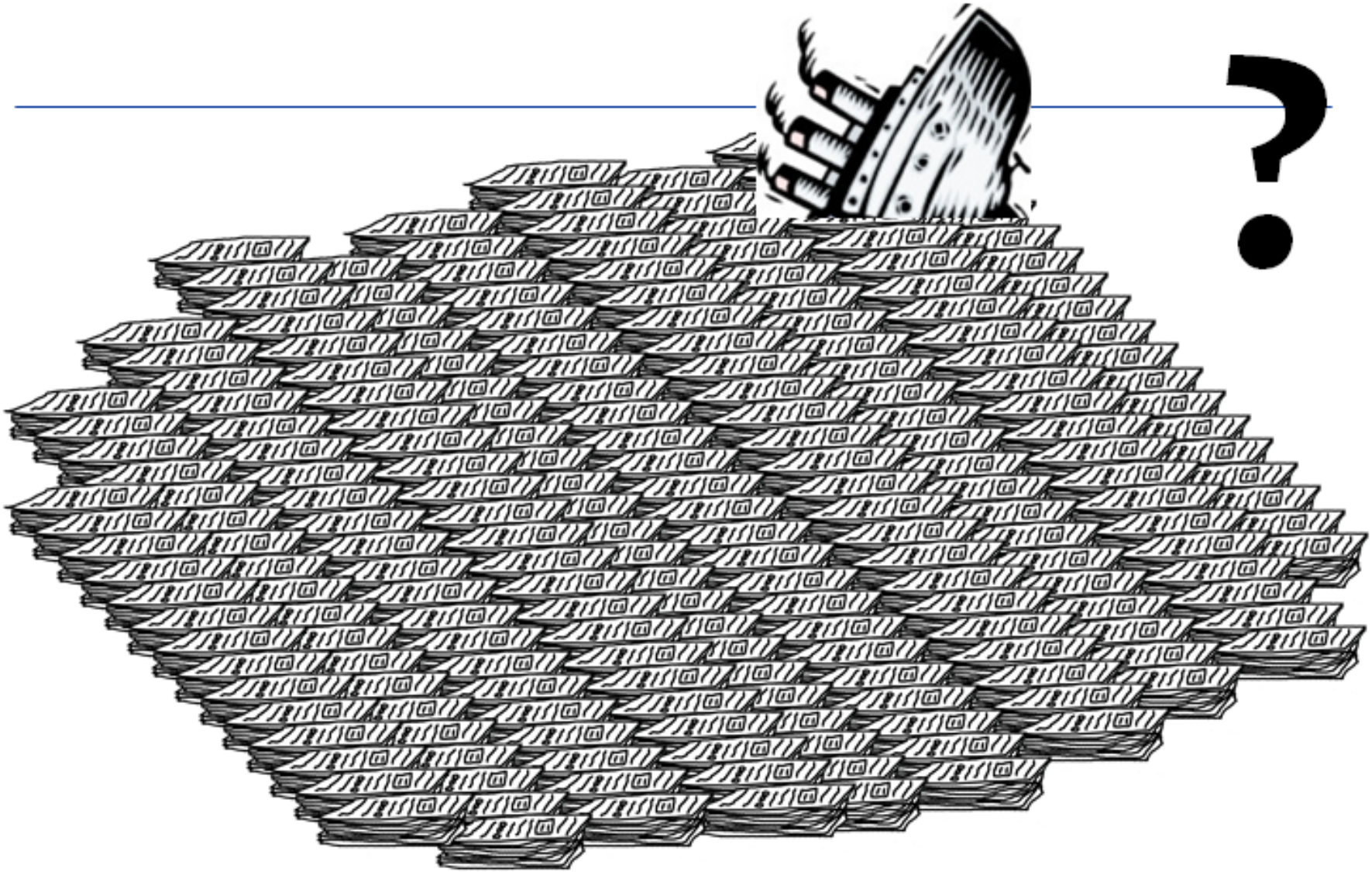

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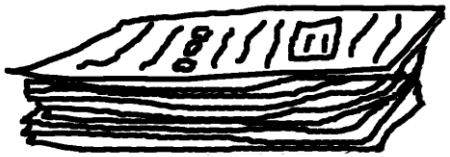
Measures of disproportionality

IC

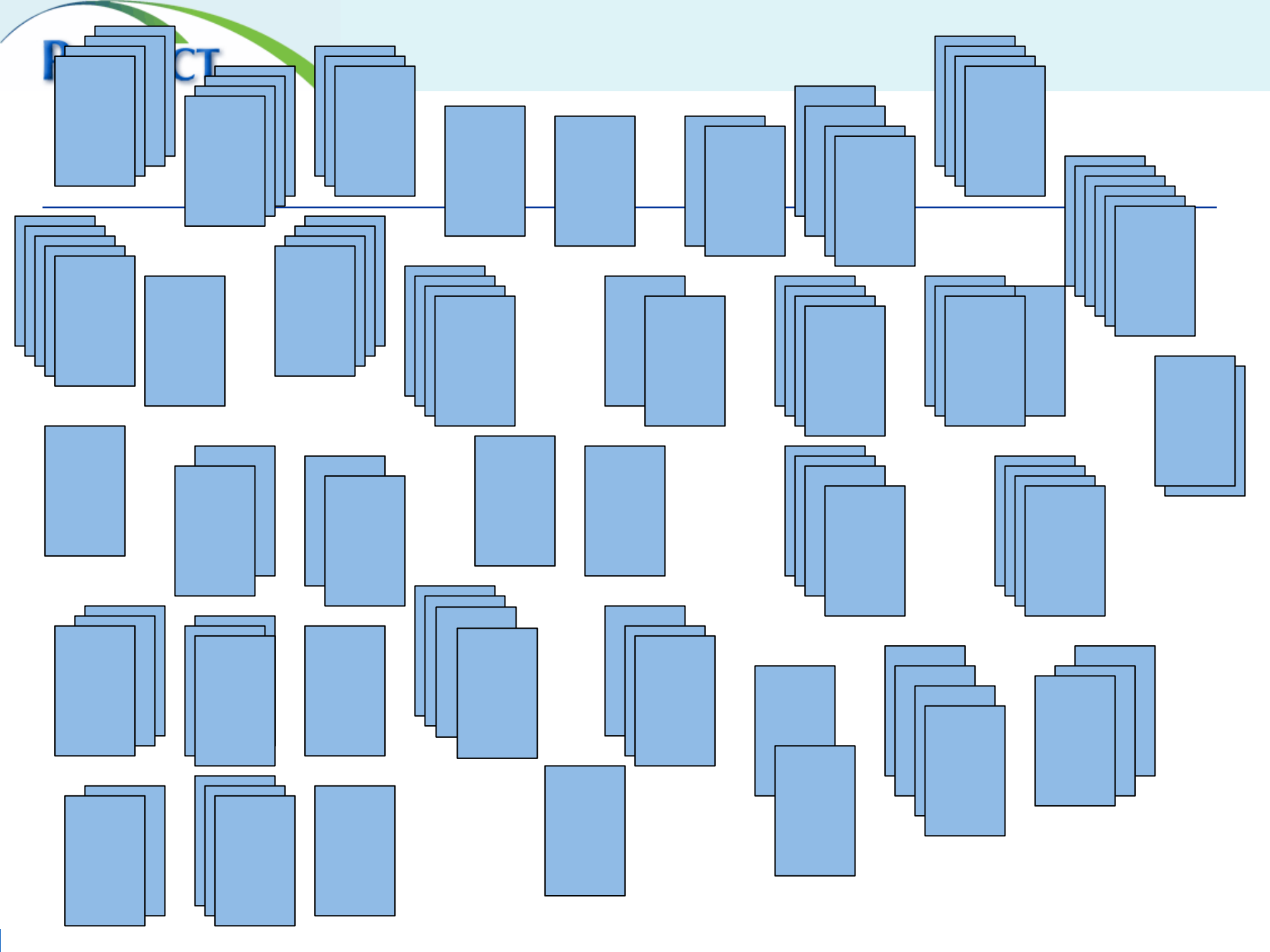
ROR



VS

EBGM

PRR



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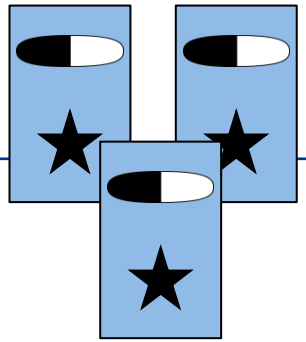

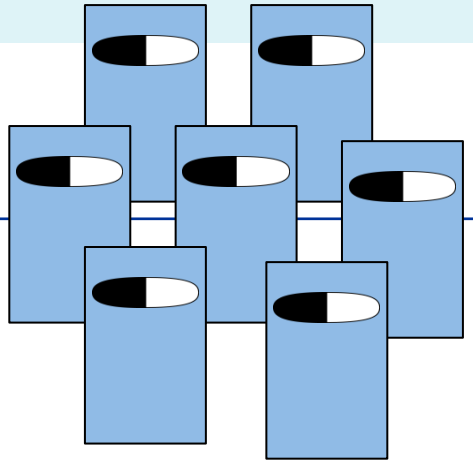

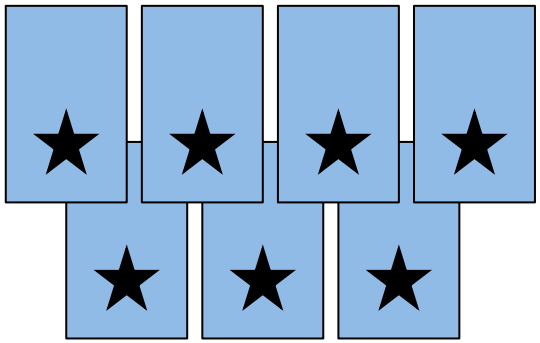

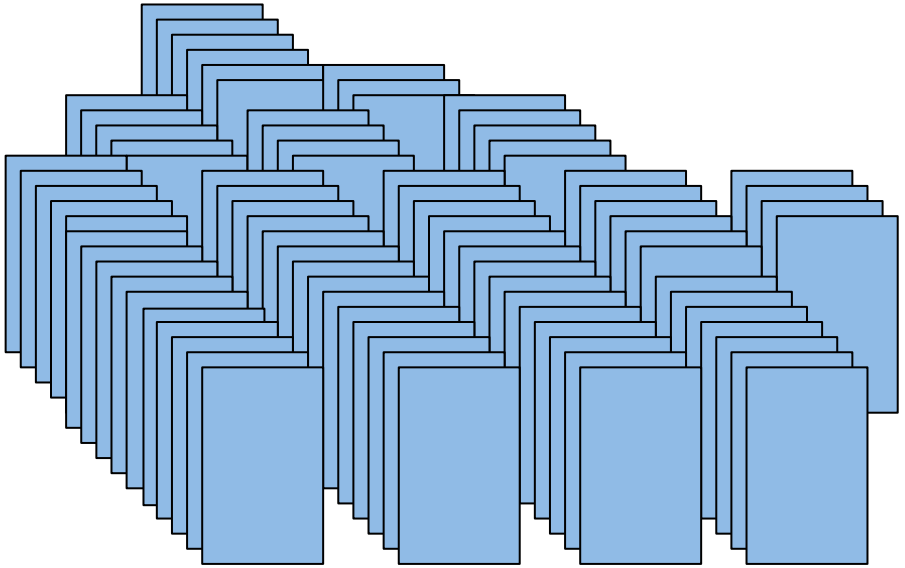

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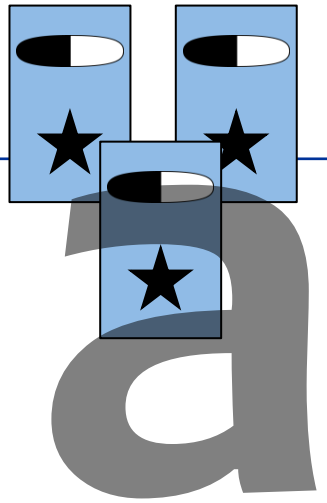
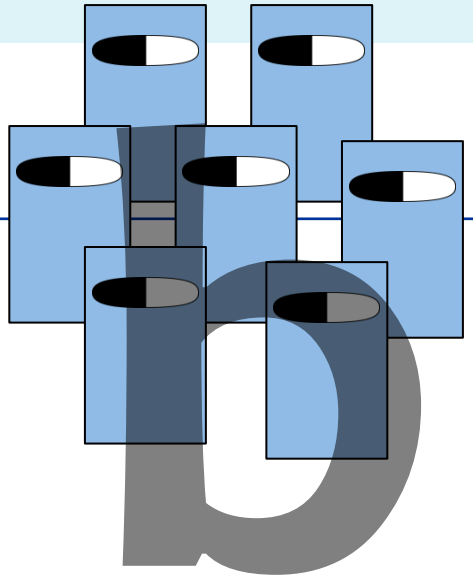
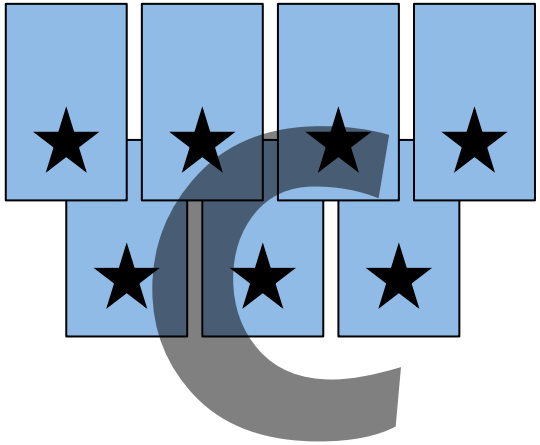
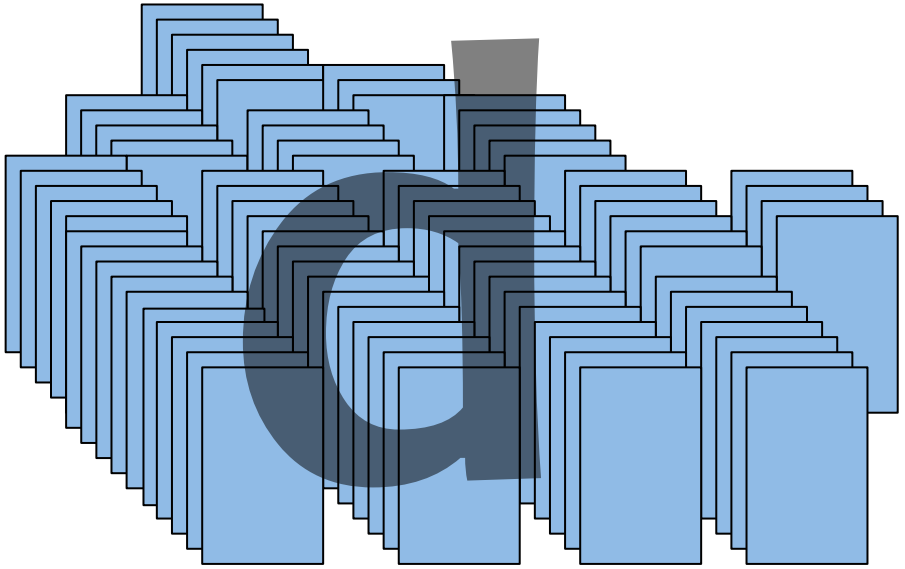
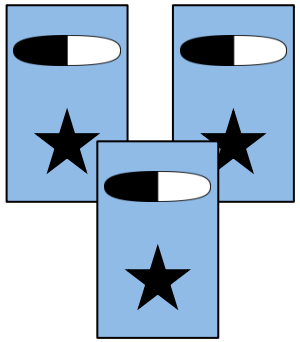




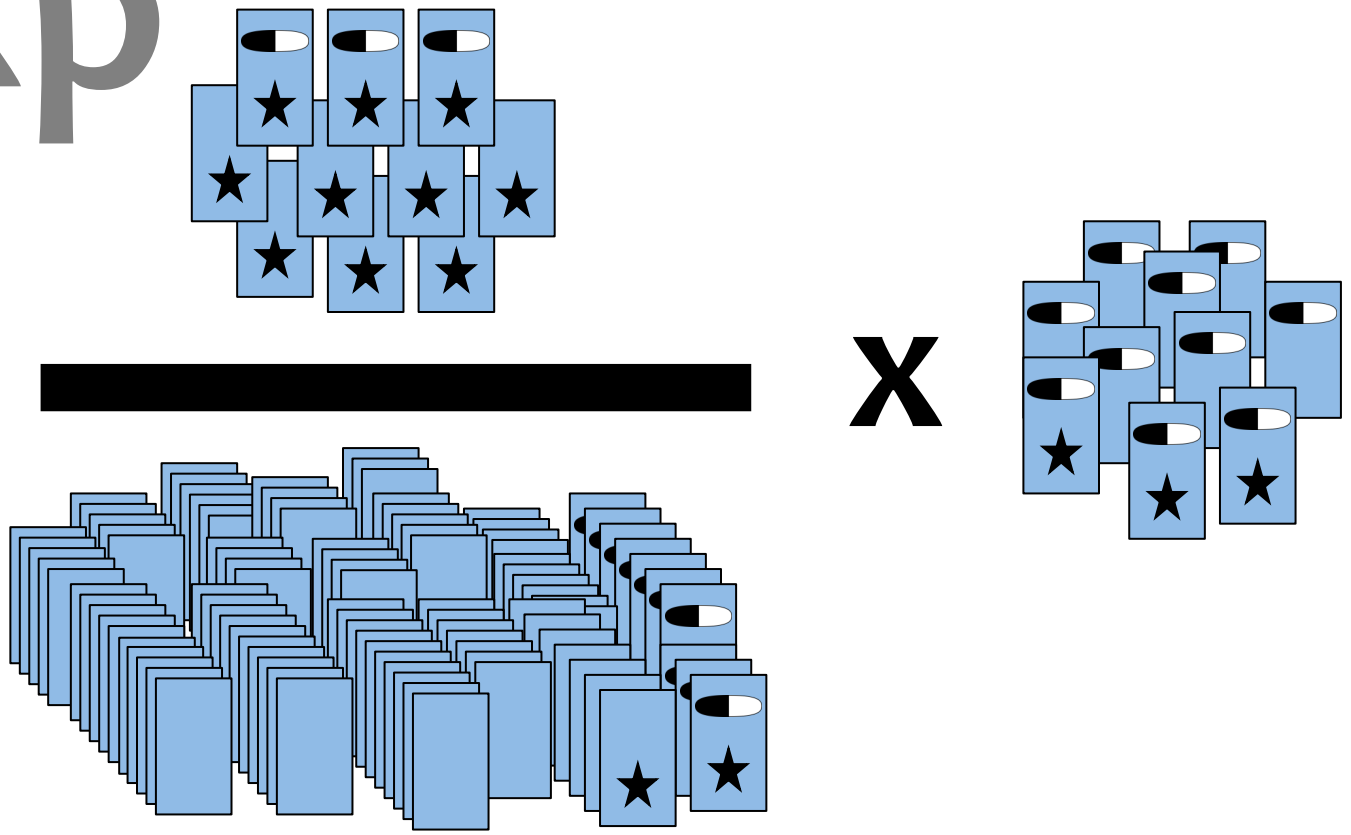




Obs= 

Exp=?

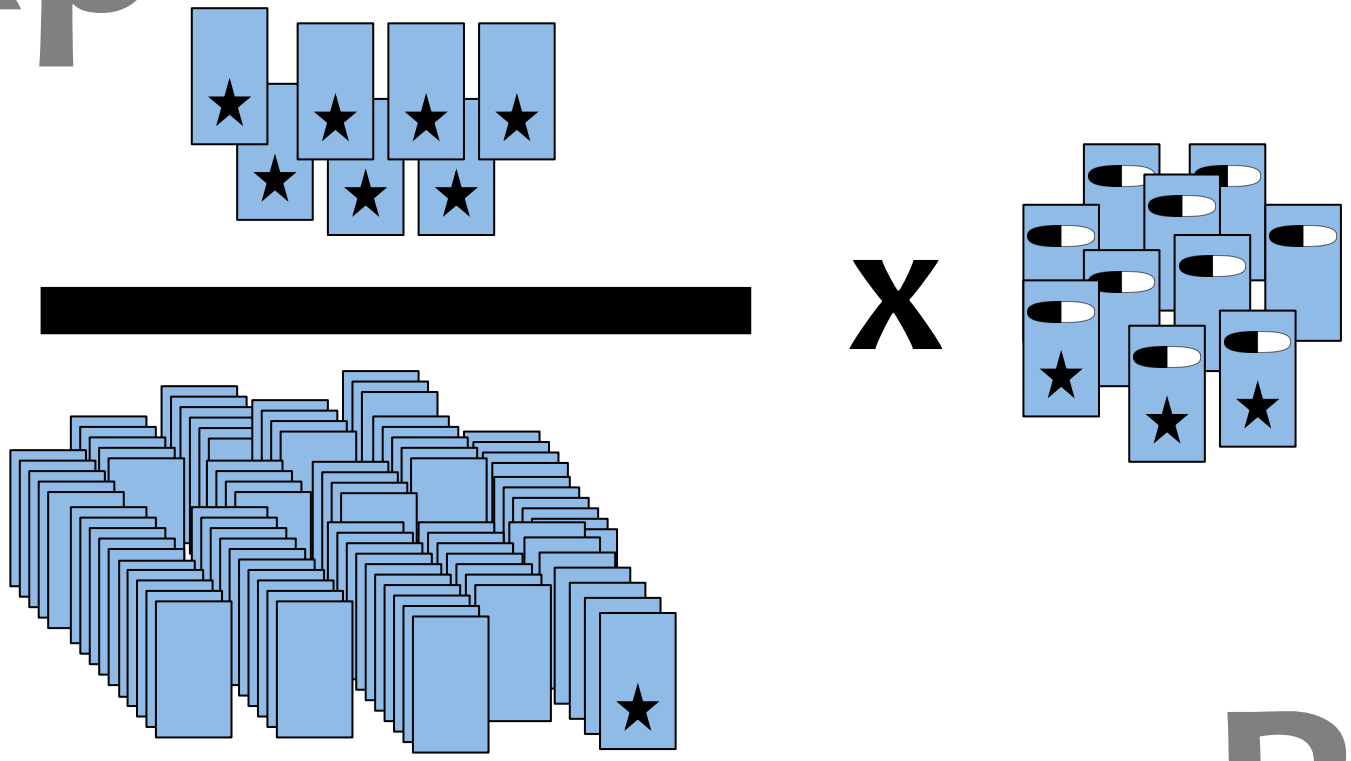
Exp



X

RR

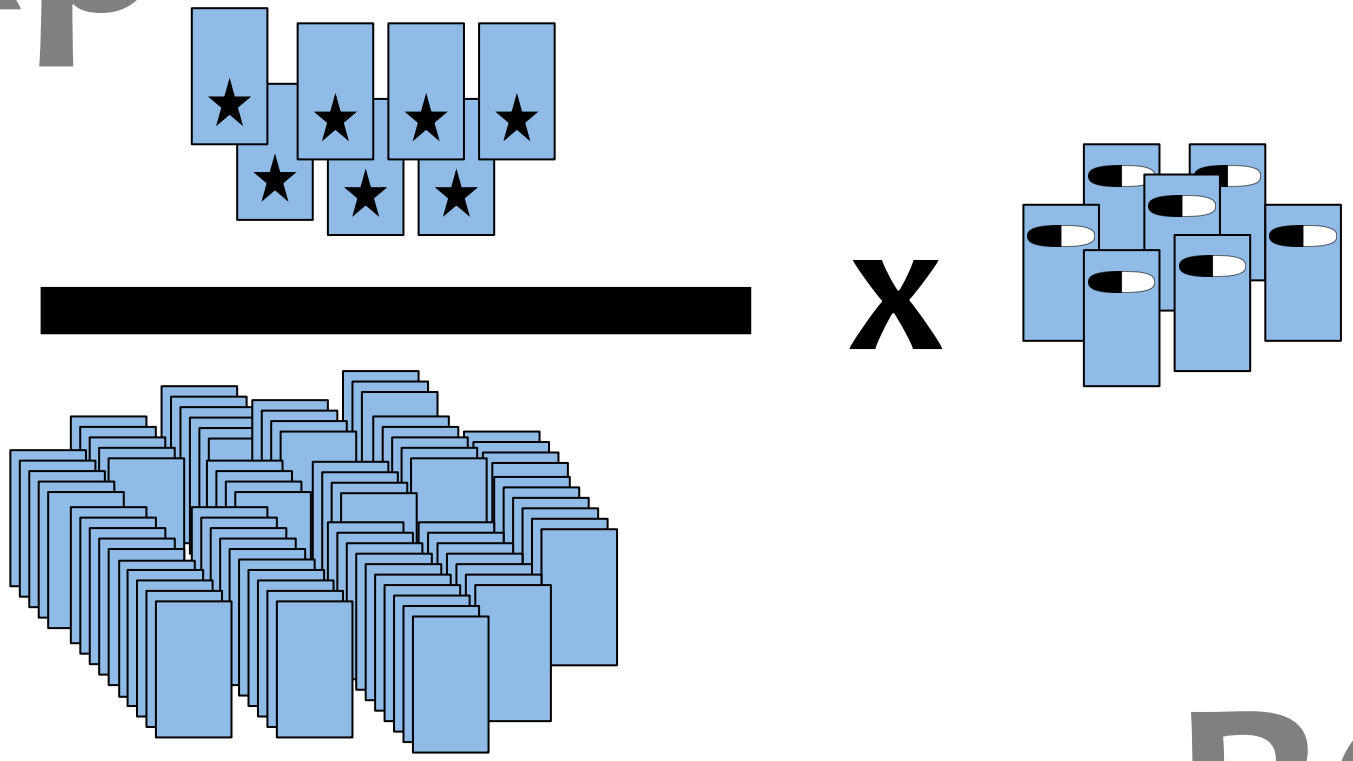
Exp



PRR

PROTECT

Exp



ROR

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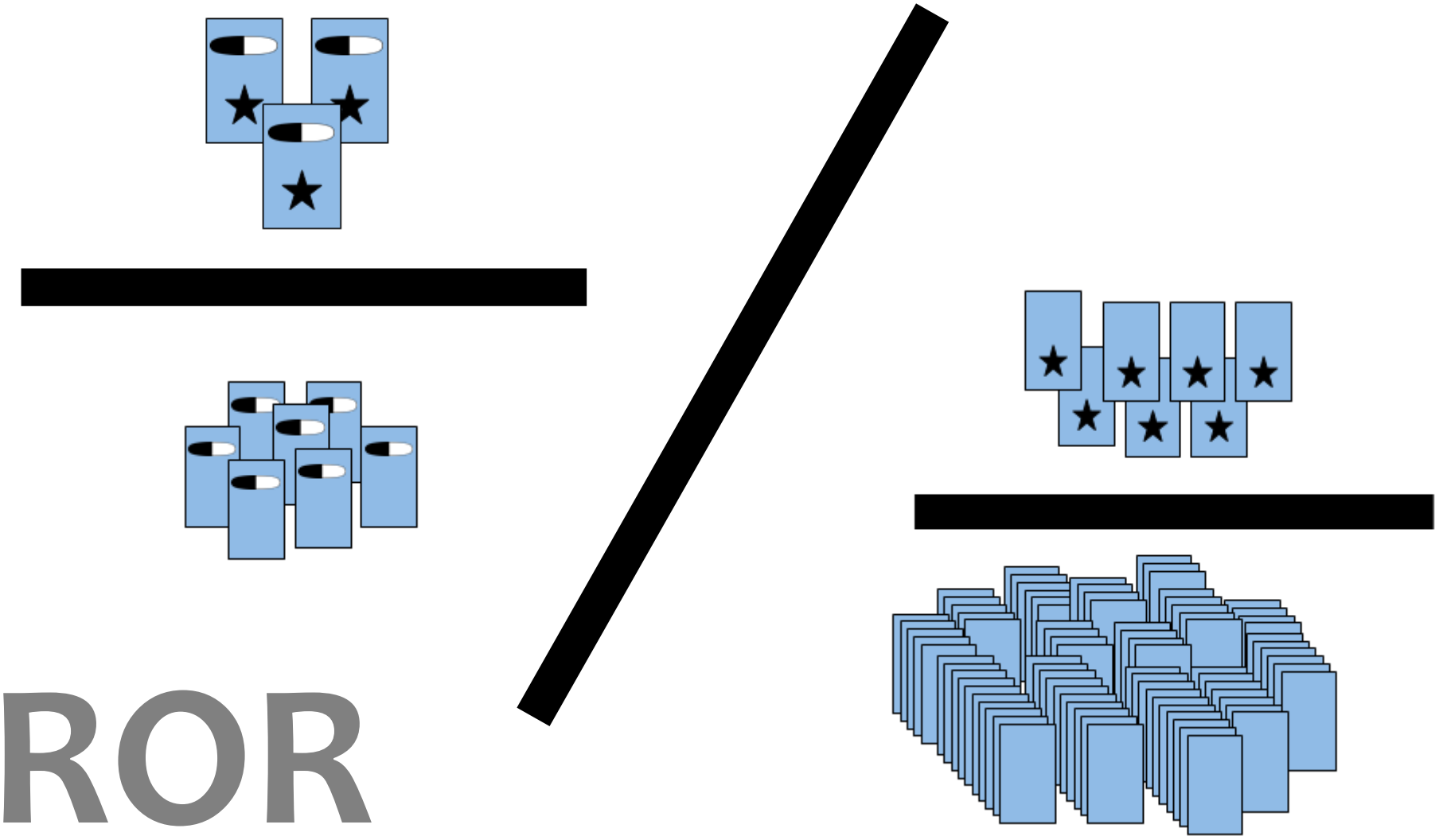

ROR

$$RR = \frac{3}{\left(\frac{(3+7)*(3+7)}{(3+7+7+83)}\right)} = 3$$

$$PRR = \frac{3}{\left(\frac{(7*(3+7)}{(7+83)}\right)} = 3.86$$

$$ROR = \frac{3}{\left(\frac{7*7}{83}\right)} = 5.08$$

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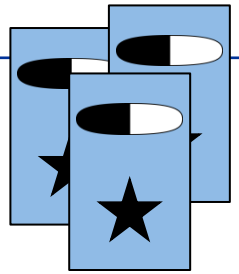
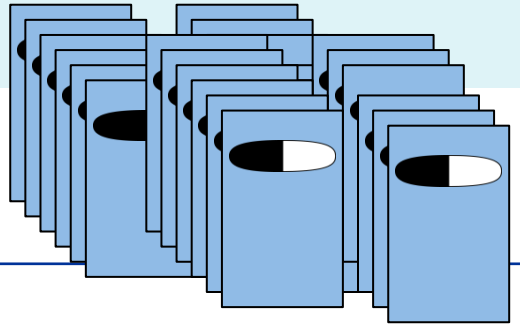


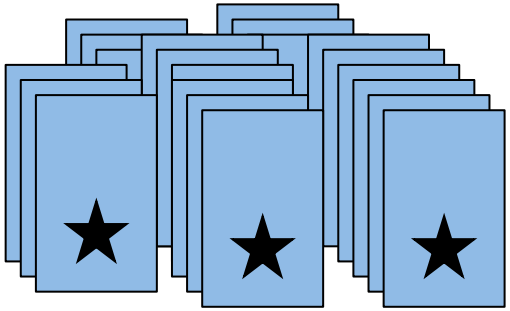
3

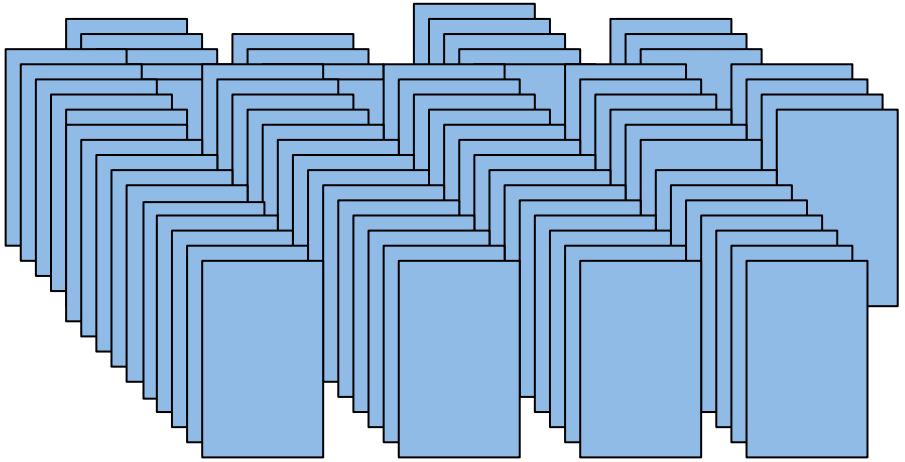


1000

1000

1 m.





$$RR = \frac{3}{(\ldots)} = 3$$

$$PRR = \frac{3}{(\ldots)} = 3.006$$

$$ROR = \frac{3}{(\ldots)} = 3.012$$

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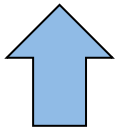
DIS-PROPORTIONAL-ITY

not



the same proportion
(of reports on the ADR)

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Which measures of disproportionality?

ROR

RR

PRR

Disproportionality and Reporting Rates

Disproportionality methods do not estimate reporting rates. No drug usage is involved in the calculation.

While reporting rates can increase for all drug-AE combinations, measures of disproportionality are interdependent:

- An increase in a measure of disproportionality for one combination causes a decrease for other related combinations

Rubber Dinghy

Rather like a rubber dinghy floating on the sea:

- if pressure causes one side to rise this causes the other to go down.
- As reports for one combination rise, this makes the expected count increase for other combinations involving the drug or the AE.

Bate MA and S. J. W. Evans -
Quantitative signal detection using spontaneous ADR reporting (2009)

How to protect against spurious associations?

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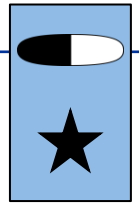
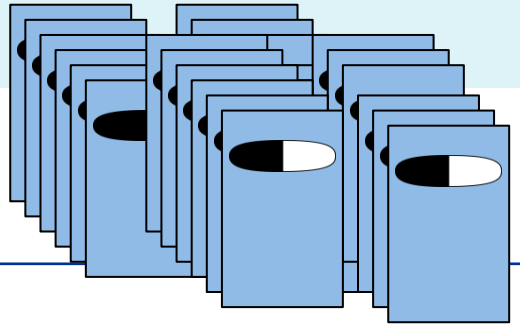


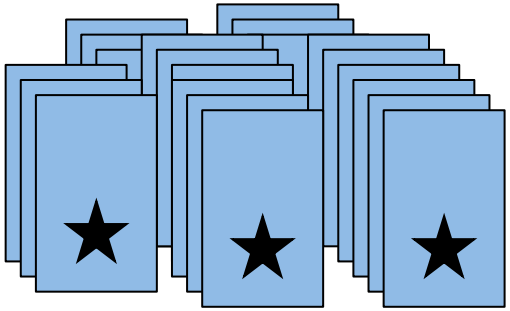
1

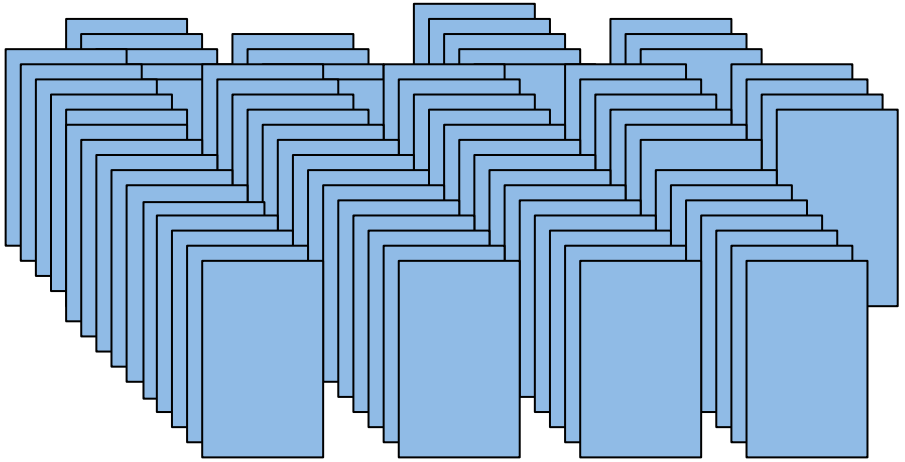


100

100

10 m.





1

VS

0.001

$$\text{RR: } \frac{1}{0.001} = 1000$$

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Simple shrinkage

$$\frac{Obs + 1/2}{Exp + 1/2}$$

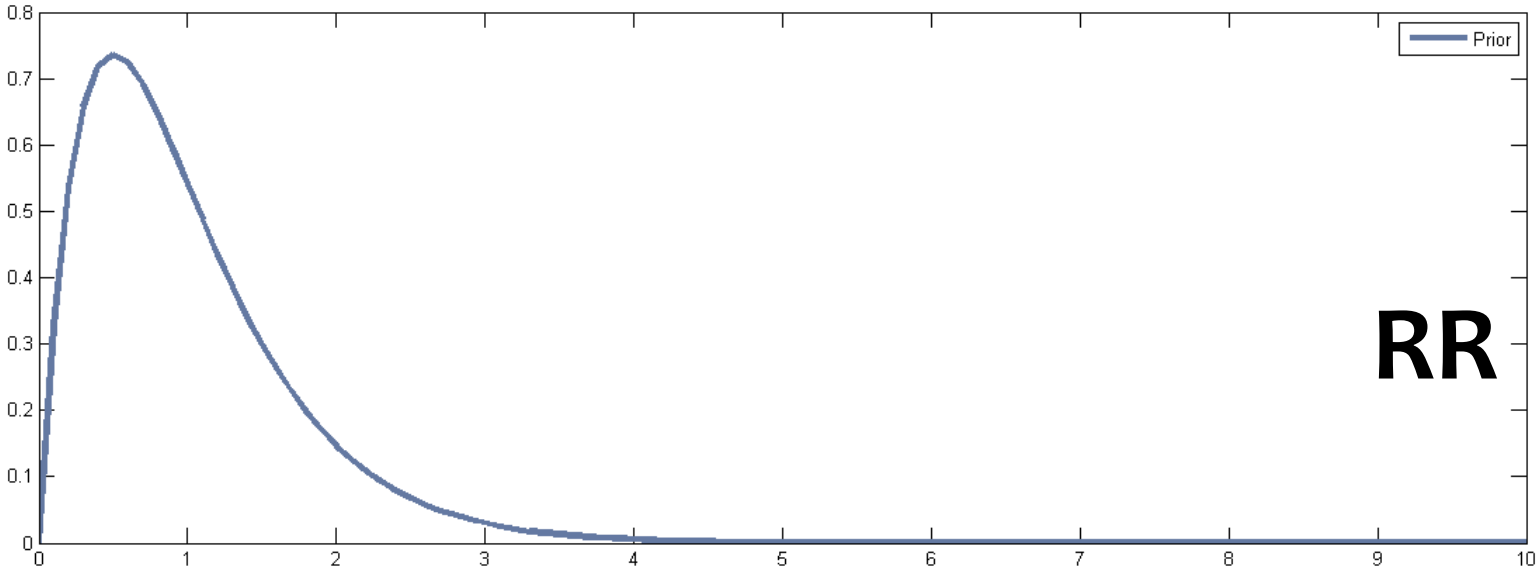
Norén et al
Stat Meth Med Res, 2011

$$\text{RR: } \frac{1}{0.001} = 1000$$

$$\frac{1+1/2}{0.001+1/2} = 3$$

Norén et al
Stat Meth Med Res, 2011

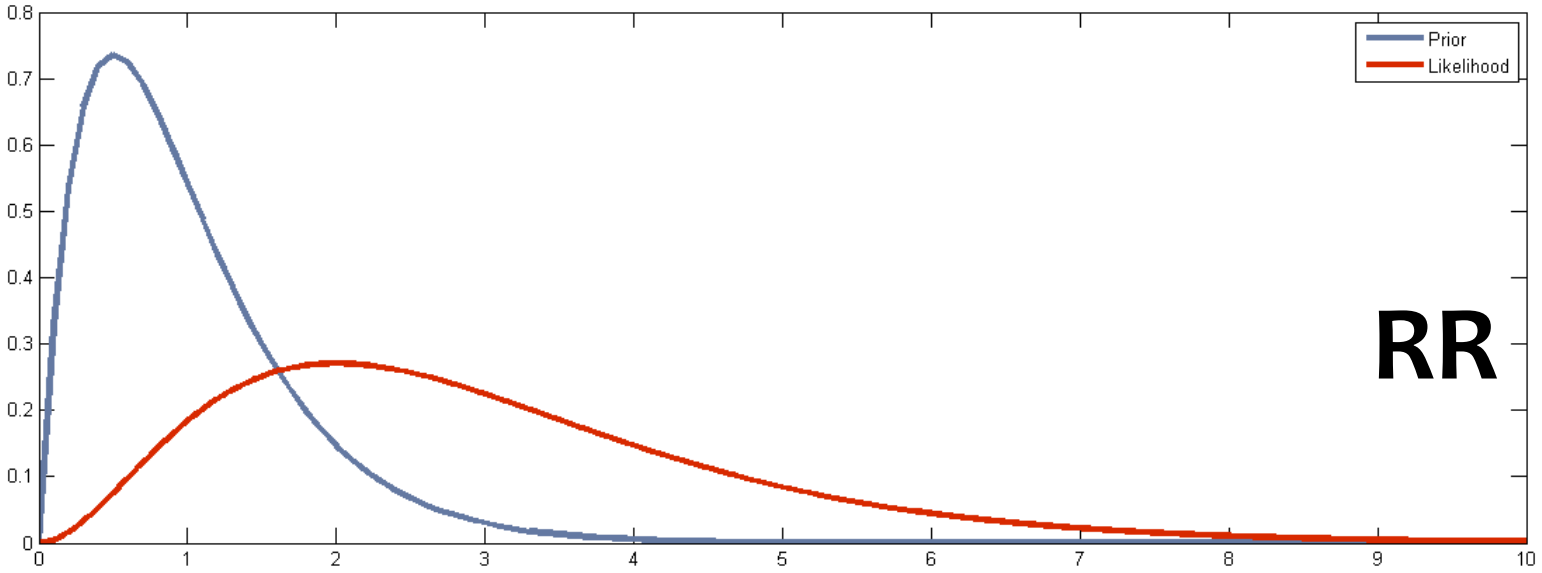
Bayesian shrinkage



Bayesian analysis: start from prior distribution

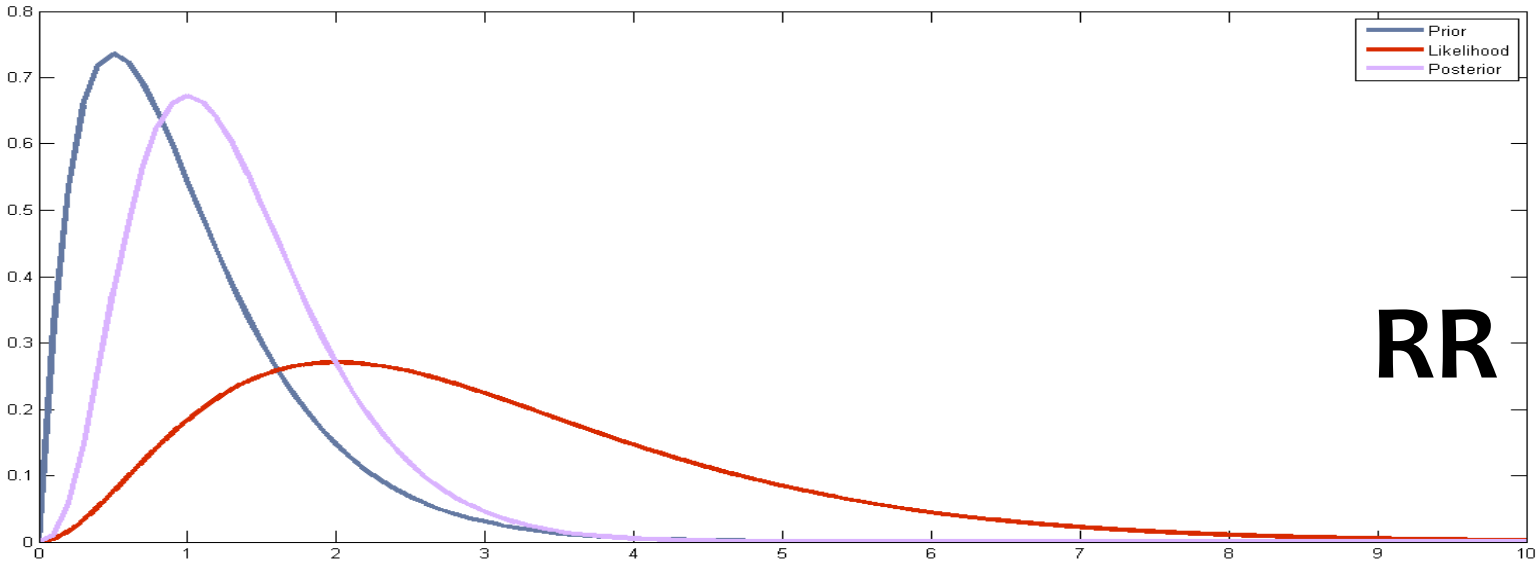
Here: our baseline assumption (until we have looked at data) is that the RR is 1 (most likely between 0.2 and 3)

Bayesian shrinkage



From data it appears that the RR is around 3

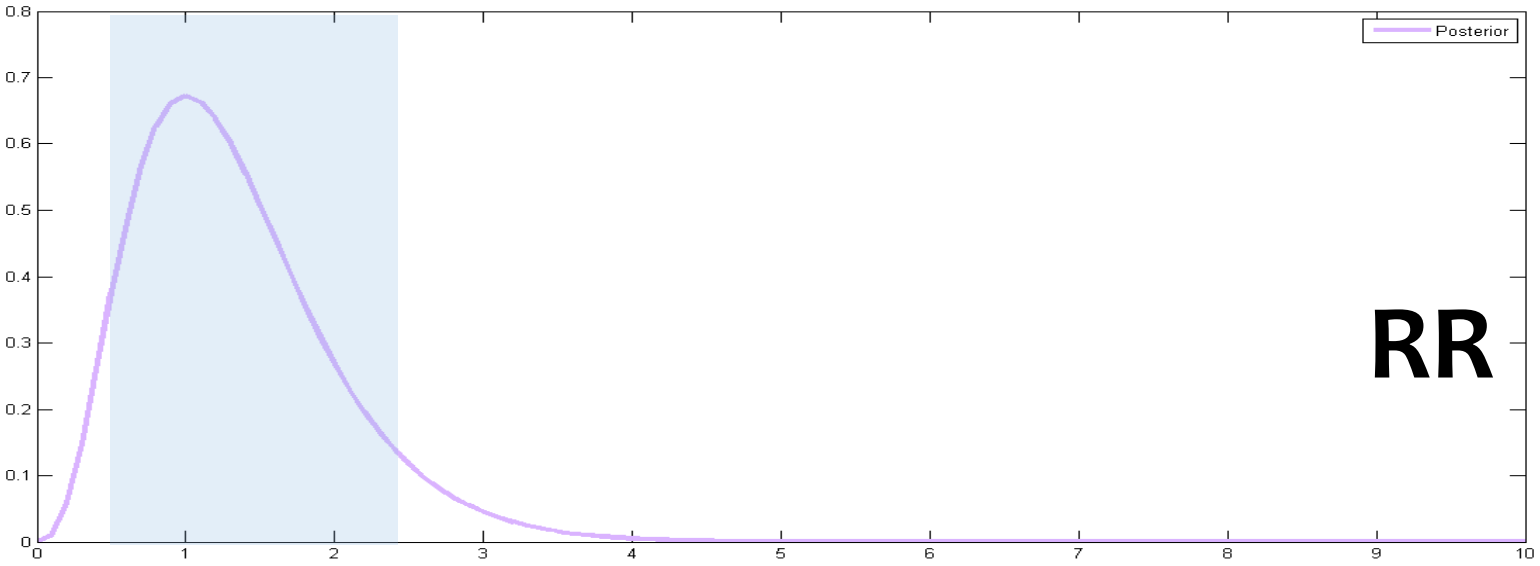
Bayesian shrinkage



Posterior distribution provides a compromise between data (likelihood) and prior

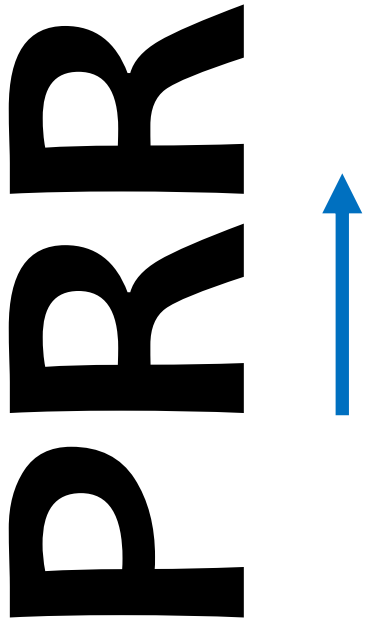
Balance between prior and likelihood depends on strength of prior and amount of data

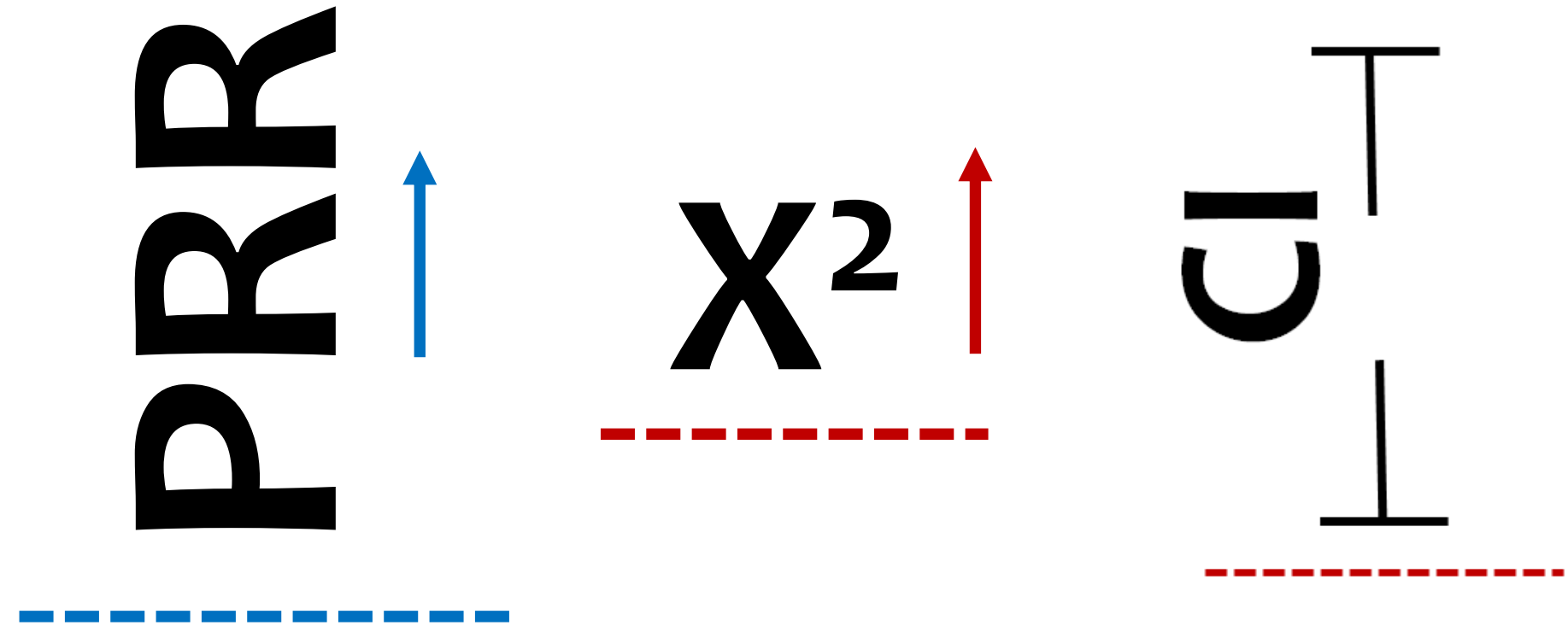
Bayesian shrinkage

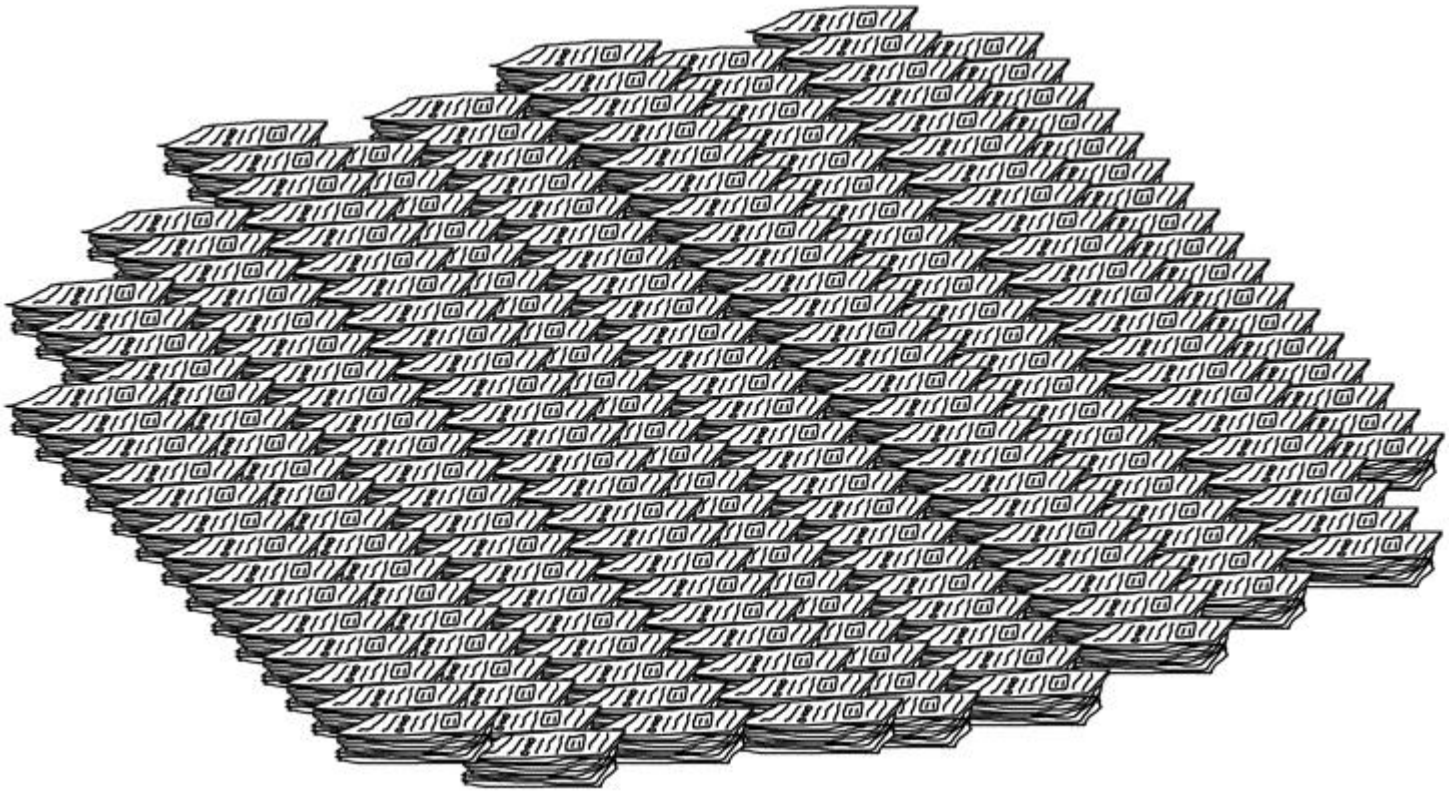


Bayesian credibility intervals provide a ‘most likely’ range for RR.

In practice used much the same way as confidence intervals.


PRR


PRR
X²
CI



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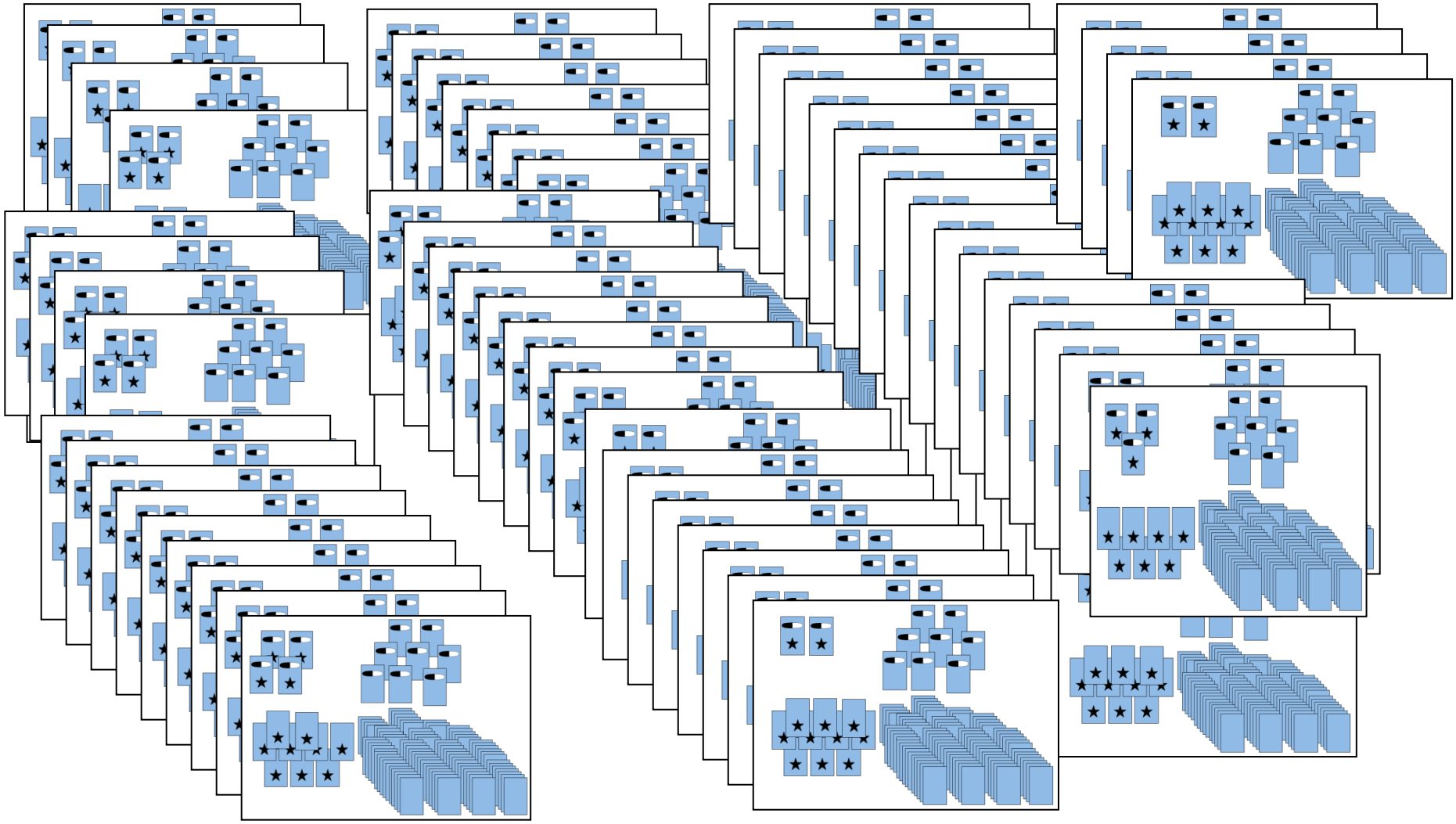
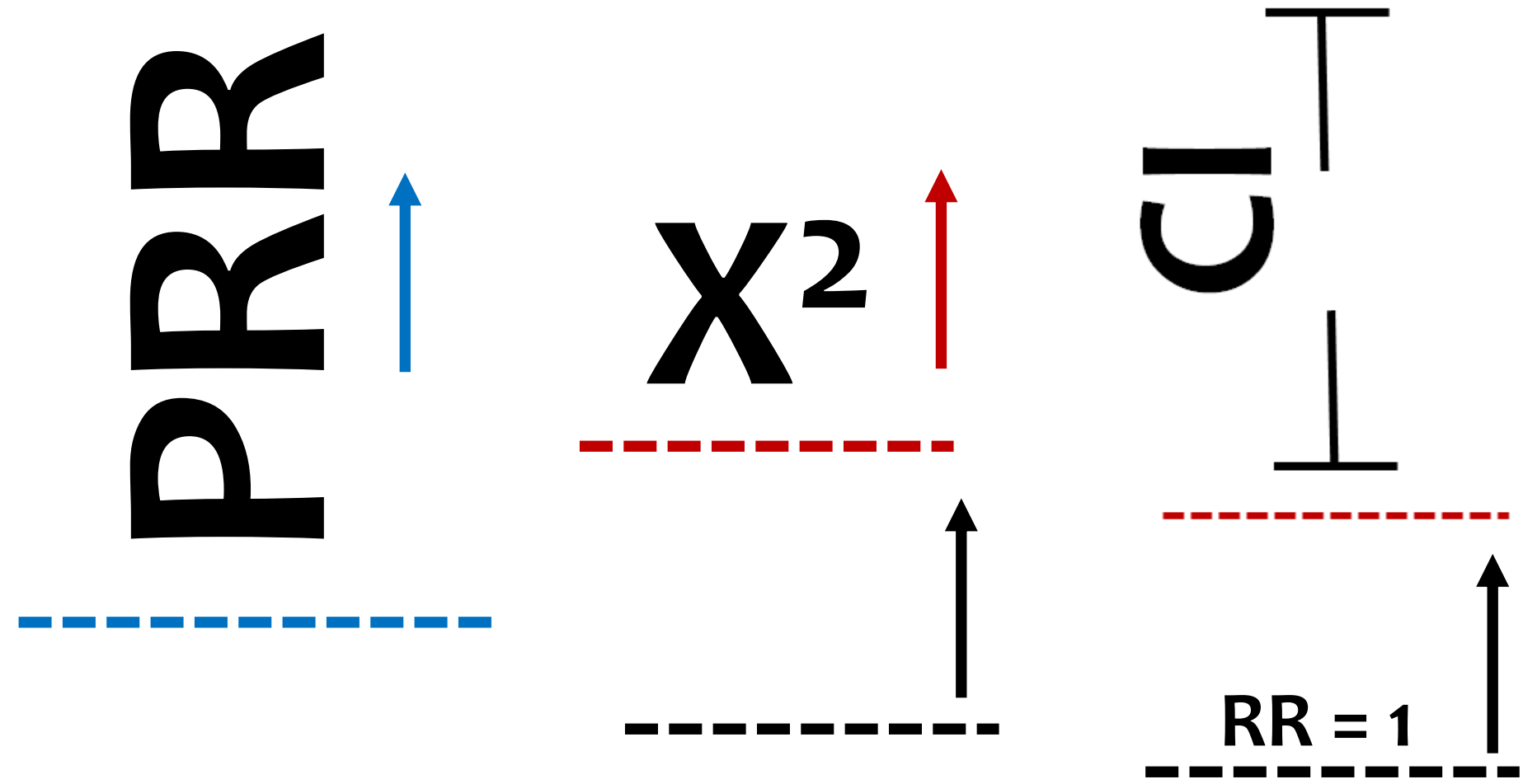
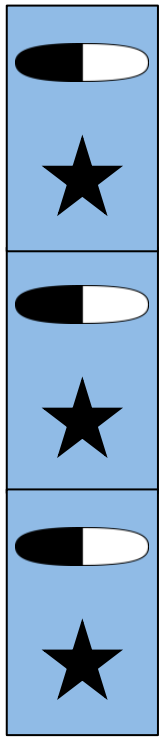



PRR
X²
CI
RR = 1

PRR ↑

X^2 ↑



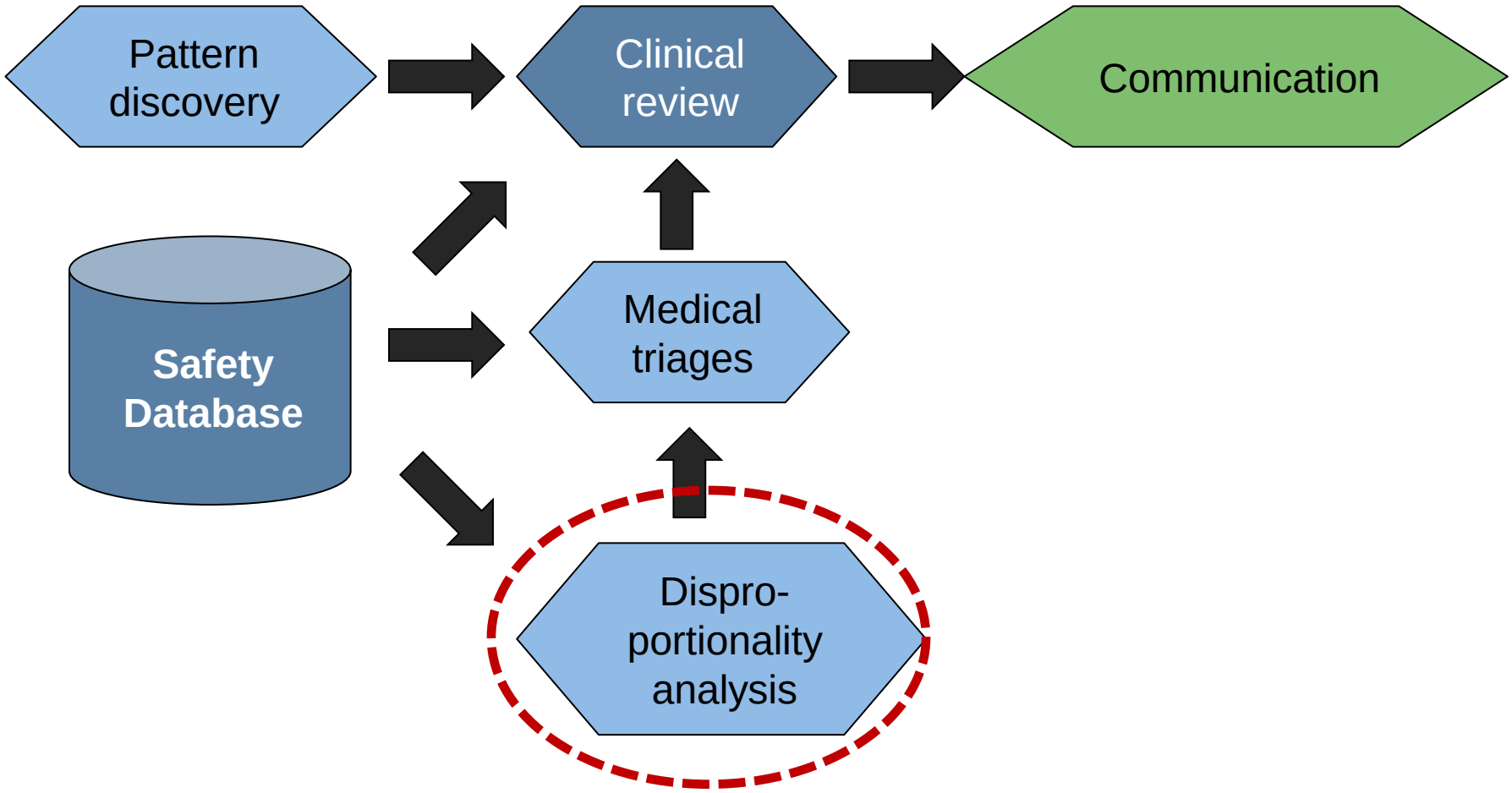
IC

ROR

EBGM

PRR

Knowledge discovery process



References

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