Are Large Samples Too Large?

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Methods for Surveillance

- Adjustment methods for surveillance

- “Late breaking” issue:

  Large vs. small effects

Methods for Surveillance

- **Propensity Scores:** Assessment of no treatment heterogeneity across PS strata

- **Instrumental Variables:** Much variability depending on the IV-treatment relationship

(>50% increase in sample size)

Large sample? N= 12,161, C=4,191

Model (Bezafibrate; risk of diabetes)	Treatment Effect (OR)	95% Confidence Interval
Logistic	0.73	(0.57, 0.92)
IV (LATE)	0.87	(0.22, 0.87)

Large sample? N= 118,397, C=8,302

Negative confounding? → Effect modification?

Model (K+ Suppl.; Arrhythmia)	Treatment Effect (HR)	95% Confidence Interval
Cox	1.22	(0.98,1.45)
Propensity Score	1.48	(0.85,1.99)

Surveillance– Active Comparators

Selection bias with respect to two active medications rather than just one.

Above PS and IV methods have not been well developed for active comparators (Jin and Rubin (2007).

Adjusting for confounding with respect to active treatments should yield even bigger increase sample sizes.

When is confounding less relevant?

With safety are selection bias factors (confounding by indication) as relevant as with effectiveness research?

Are large effects less vulnerable to confounding than small effects?

What is a large effect?

What measures do we use in pre-approval studies of efficacy?

Number-Needed-to-Treat (NNT)

Can we translate to surveillance?

Number-Needed-to-Harm (NNH)

NNH= NNT/2 ?