



Statistical Methodology
Clinical Development

Discussion on Extrapolation

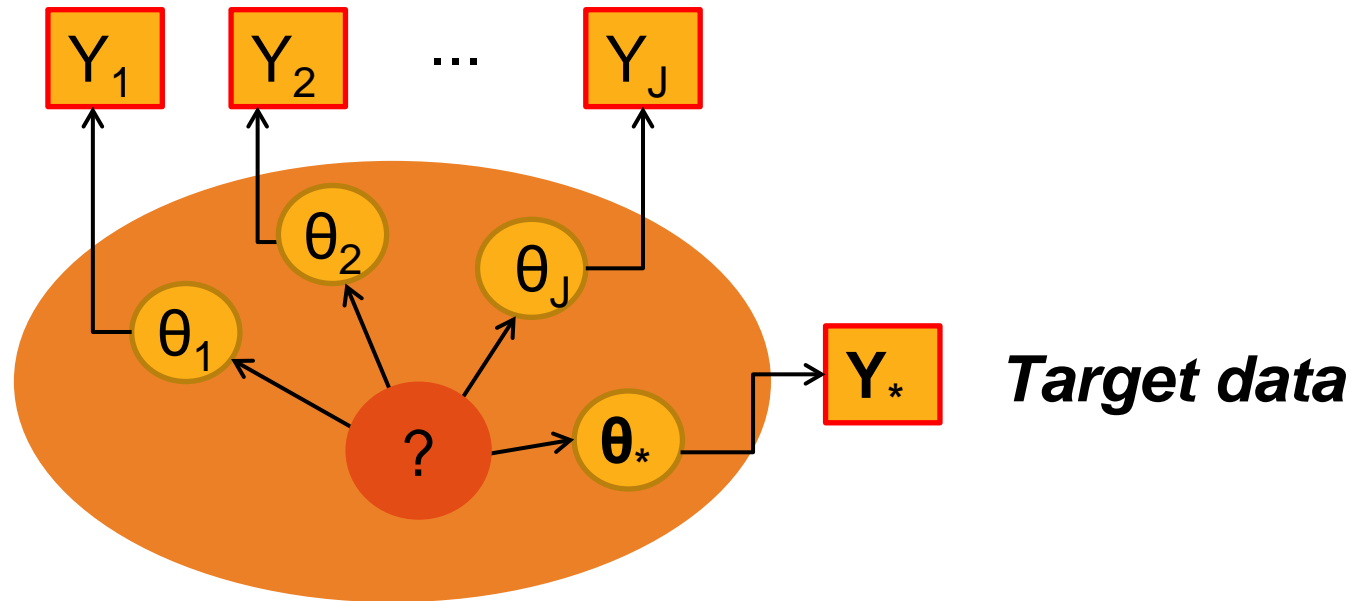
Heinz Schmidli

*FP7 Small-population research methods projects
and regulatory application workshop*

London 29-30 March 2017

Evidence Synthesis and Extrapolation

Source data



- Borrowing strength by linking parameters
- Robust extrapolation for decision making and design
- Bayesian framework natural for inference/prediction

Borrowing strength and Robustness

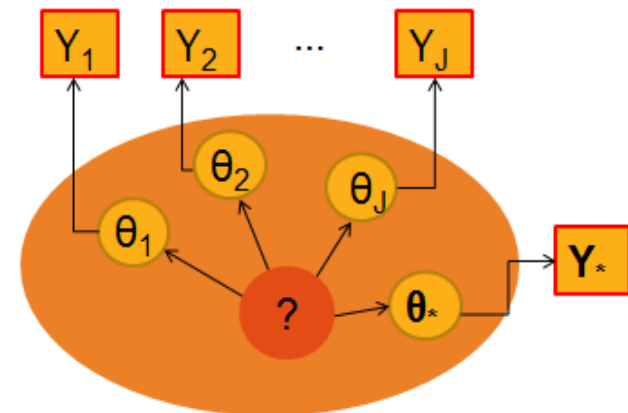
Borrowing strength by linking parameters

- **Test and Pool**

Yes/No *Holger Dette*

- **Hierarchical models**

Gradual *Sarah Zohar*



Robustness

Possibility that source data may not be relevant

Prior probability for scepticism *Franz König*

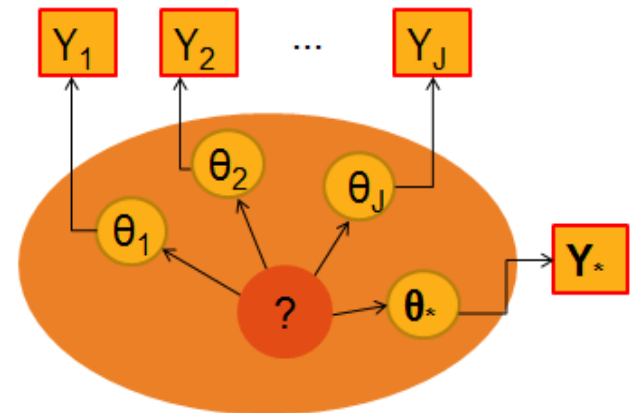
FDA (2016) Leveraging existing clinical data for extrapolation to pediatric uses of medical devices.

Schmidli H et al. (2014) *Biometrics*

Decision making and Design

Clinical development

- ***Data from various phases***
Pre-clinical, phase I, II, III, ...
- ***Data from different populations***
Adult/pediatric, disease subtypes, ...



Sequentially available data used for

- ***Stop/go decisions***
- ***Design of future trials***

"... design is a decision problem. Introduction of some kind of prior information can hardly be avoided." DR Cox

Neuenschwander et al. (2016) *Statistics in Biopharmaceutical Research*