Medicines & Healthcare products Regulatory Agency

MHRA
Regulating Medicines and Medical Devices

Statisticians perspectives on extrapolation

Dr David Wright Expert Statistical Assessor MHRA

Chair BSWP

Content

- How can Statistics help in extrapolation
- Different approaches

How can Statistics help?

- Help develop a structured framework to enable more informed decisions on when it is appropriate to extrapolate to be made.
- Help summarise information already available. For example, integrate evidence via a meta-analysis.
- Evaluate whether the use of different methods leads to the regulatory hurdle to demonstrate a positive benefit risk being altered.

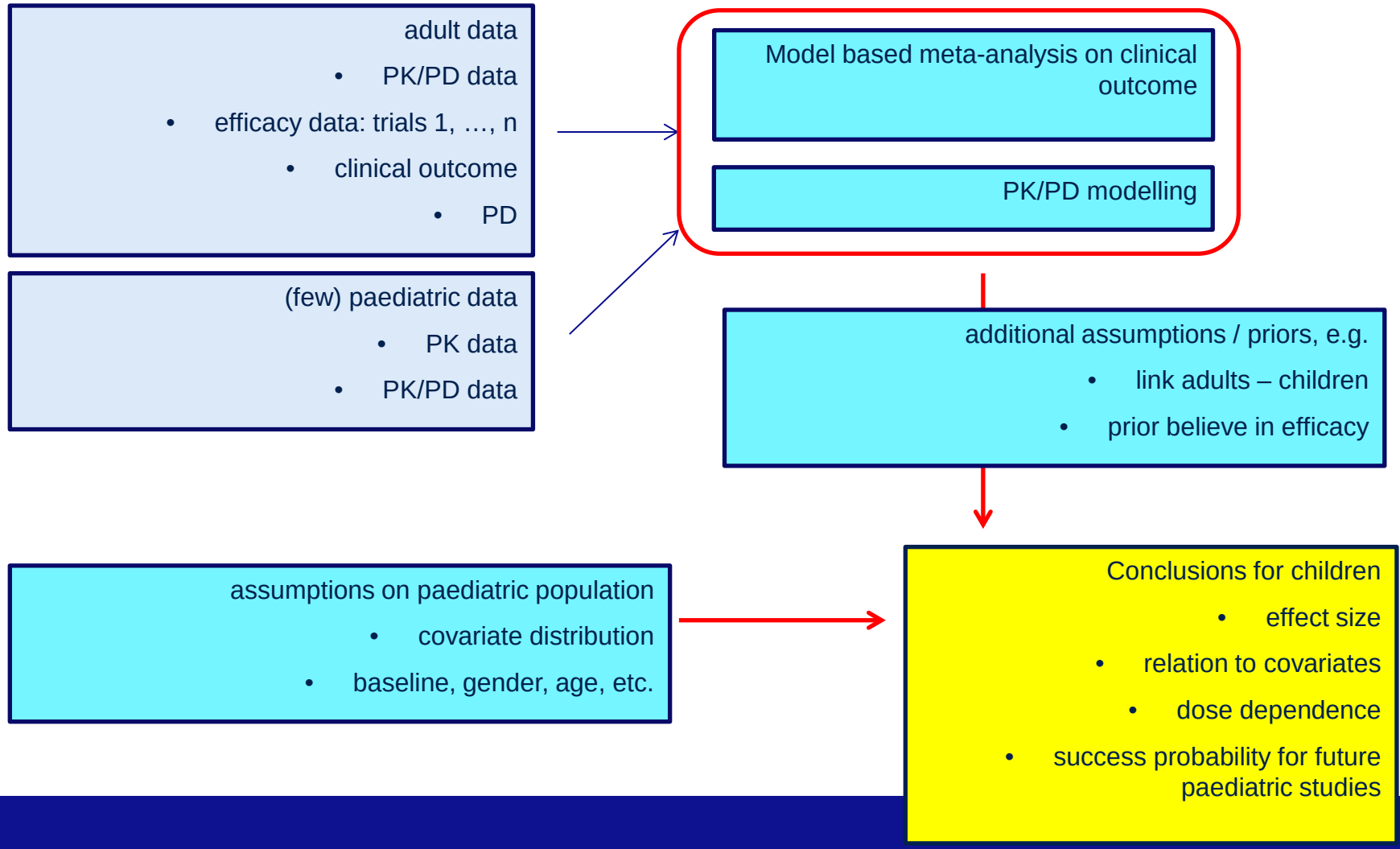
Why develop a structured framework?

- Sometimes discussions about whether or not to allow extrapolation of data from one patient population to another lacks specific criteria to enable other stakeholders the ability to understand why extrapolation has been allowed or not in a particular circumstance.
- Providing a structure will reduce the potential for misunderstanding of why some feel that extrapolation is not possible whereas other are comfortable with allowing it.

Help summarise information already available

- This is a part of a statistician’s day to day work. For example meta-analysis.
- Summary of efficacy forms an important part of a Centralised assessment.
- Challenges
  - Incorporating information from different sources (e.g. clinical trials in adults and PK/PD trials in adults and children)

Extrapolation strategy (example)



Different possible approaches

- Conduct an underpowered randomised study
- Define a success criteria that is easier to meet (higher Type I error) taking into account information from other populations
- Bayesian methods
- Use a different (maybe a surrogate) endpoint

Use of modelling in extrapolation

- To inform the design of a confirmatory clinical study (not controversial)
- To decide a confirmatory clinical study is not required (controversial)
- To decide that an abbreviated confirmatory study could be acceptable (for discussion) – could use framework such as that proposed by Martin Posch to decide whether an abbreviated development is possible.