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Does size matter? : bridging and dose selection in paediatric trials

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Propositions to the doctoral thesis

‘Does size matter? Bridging and dose selection in paediatric trials’

1. Traditional approaches for dose selection do not guarantee minimal conditions for bridging between adults and children: the paediatric dose is not scaled for function. *This thesis*
2. The correlation between dose and demographic covariates is not linear. *This thesis*
3. In a pharmacokinetic study with sparse sampling of drug concentrations the number of children is more important than the number of samples per subject. *This thesis*
4. The inclusion of priors from model parameters in adults allows for inferences about the clinical relevance of pharmacokinetic differences across paediatric populations. *This thesis*
5. Model predictions based on maximum likelihood methods are valid as long as the same parameter distributions can be warranted across the populations of interest. *This thesis*
6. The difference between goodness-of-fit and goodness-of-prediction is as subtle as the difference between homicide and suicide. *Karlsson, Forensic Sci. Int., 1999*
7. The uncertainty owing to both the sampling variability and the choice of model(s) should be given when modelling results are presented. *Vock et al., Bull. World Health Organ. 2011*
8. Fixed-dose co-formulations offer logistic and adherence advantages (*Kauss et al., Int. J. Pharm. 2010*). However, their use in clinical trials ignores the implications of inter-individual variability in pharmacokinetics.
9. The view that “children are mature and differ from adults only in size - children are small adults, from a PK perspective” (*Holford, Clin. Pharmacol. Ther. 2009*) is not warranted.
10. For many, statistics are numbers to which complex mathematical formulæ can be applied to produce conclusions of dubious veracity from which all wit and human life is rigorously excluded. *James Le Fanu, “The Rise and Fall of Modern Medicine”, 2000*
11. Failure is not fatal, but failure to change might be. *John Wooden, UCLA coach 1948-1975*
12. I’ve got a theory that if you give 100% all of the time, somehow things will work out in the end. *Larry Bird*