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Influence of mathematical model structure on the estimation of phamacokinetic parameters : the example of Vdss

The steady-state volume of distribution (Vdss) is an important pharmacokinetic (PK) parameter that is used to estimate the drug efficacy and toxicity. However, non-compartmental analysis (NCA), based on mammillary models with central linear elimination, is still at the heart of the primary method to estimate this parameter.

However, the suitability of this NCA approach is questioned for complex drug eliminations, as it is the case for simultaneous first-order and Michaelis-Menten eliminations.

In this talk I will discuss two indistinguishable PK models having a structure of two compartments and different elimination pathways.

As results I will show the corresponding exact model based expressions of Vdss directly derived from its physiological definition and discuss their relationship to the NCA counterparts. As proof of concept, the important difference will be shown on various real drug models.

Moreover, considering the issue of model identifiability, the evaluation of Vdss will be discussed.

This is a joint work with X.T. Wu and F. Nekka