

Stellingen behorende bij het proefschrift

**Dosing Optimization of Beta-Lactam Antibiotics
using Parametric and Nonparametric Population Pharmacokinetic Models**

1. A coordinated redevelopment procedure for dosing optimization of old antibiotics using PK/PD principles is urgently needed, with a particular priority to the reassessment of PK/PD targets for efficacy, resistance and toxicity. (*this thesis*)
2. Clinical studies aiming to correlate PK/PD indices with outcomes in patients are more necessary than studies investigating the effect of TDM on clinical outcomes (*this thesis*)
3. A complete pharmacometric analysis should be performed for all new antibiotics during drug development. (*this thesis*)
4. Twice daily high dosing as an alternative to three times daily low dosing should be removed from the summary of product characteristics of amoxicillin. (*this thesis*)
5. Nonparametric models show a higher between-subject variability of parameters compared to parametric models. (*this thesis*)
6. Using a single MIC determination for antibiotic dosing adjustment based on TDM is inappropriate. (*Johan W. Mouton et al, J Antimicrob Chemother 2018;73:564-8*)
7. As antibiotic dose adjustments based on eGFR increase the risk of treatment failure and death, the use of the full dose of the antibiotic should be considered when the only strategy available for adjustment is based on the eGFR. (*Marianne S. Camargo et al, Eur J Clin Pharmacol 2019;75:119-26*)
8. Dosing adjustments for renally impaired patients should be based on BSA-unadjusted eGFR (ml/min) instead of BSA-adjusted eGFR (ml/min/1.73 m²). (*KDIGO 2012 Clinical practice guideline for the evaluation and management of CKD. EMA/CHMP/83874/2014*)
9. We ought to prescribe therapeutic drugs to our patients with the finesse of a surgeon's scalpel, rather than clumsily bludgeoning every patient with the same sledgehammer-like dose. (*Michael Neely, Clin Pharmacol Ther 2017;101:368-72*)
10. It is more important to know what sort of person has a disease than to know what sort of disease a person has. (*Hippocrates, 460-377 BC*)
11. Alles, was man tun muss, ist die richtige Taste zum richtigen Zeitpunkt zu treffen, und das Instrument spielt von ganz allein. / All you have to do, is touch the right key at the right time and the instrument will play itself. (*Johann Sebastian Bach, 1685-1750*)