The role of glomerular filtration and active tubular secretion in predicting renal clearance of drugs in children using population pharmacokinetic and physiology-based pharmacokinetic modeling approaches: unspinning the yarn

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Stellingen behorende bij het proefschrift

The role of glomerular filtration and active tubular secretion in predicting renal clearance of drugs in children using population pharmacokinetic and physiology-based pharmacokinetic modeling approaches

Unspinning the yarn

1. Model-driven dose optimization supports an effective and safe treatment from the start of therapy in special populations. *This thesis*
2. PBPK principles are a prerequisite to establish guidelines for dosing renally excreted drugs in children for drugs with various properties. *This thesis*
3. Knowing the unbound drug fraction in adults is essential to accurately scale pediatric drug doses by the maturation function of glomerular filtration rate for drugs mainly eliminated by glomerular filtration. *This thesis*
4. Ignoring the ontogeny of renal transporters for children younger than 2 years leads to inaccurate renal clearance predictions for drugs that are mainly eliminated by active tubular secretion. *This thesis*
5. Transporter ontogeny functions that cannot be measured *in vivo* can be derived from pediatric PK profiles by combining mechanistic insight of PBPK models with population PK estimation methods. *This thesis*
6. Trough concentrations are overemphasized as surrogates for safe and effective antibiotic exposure and treatment. *Modified from Neely, 2013*
7. For drugs that are being subject to active tubular secretion the proportionality between unbound drug fraction and renal clearance changes with extraction ratio as a consequence of the blood flow limitation. *Modified from Levy, 1980*
8. The audience for nifty modeling methods and techniques is not as large as the audience that would benefit from understanding and applying model-informed precision dosing in the clinic. *Modified from Henning, 2020*
9. Following up on the work of others can be more of a challenge than a head-start.
10. Great colleagues who cook well are an asset to any office.
11. Never look into your modelling results as in the mirror of Erised. *Modified from Harry Potter*
12. The right data are indispensable for a good model. The right analysis methods and the right graphics are indispensable for a good modeler. *Modified from Vandemeulebroecke 2019*

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