The handle http://hdl.handle.net/1887/67291 holds various files of this Leiden University dissertation.

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**Title:** First-pass and systemic metabolism of cytochrome P450 3A substrates in neonates, infants, and children  
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1. Inflammation and organ failure lead to an increased exposure to CYP3A substrates in critically ill children. *This thesis*

2. Intestinal and hepatic CYP3A activity can be quantified by application of advanced physiological population pharmacokinetic modelling approaches. *This thesis*

3. The very low presystemic and systemic metabolism of midazolam in preterm neonates is due to immature CYP3A activity not only in the liver, but also in the gut wall. *This thesis*

4. Clearance of most CYP3A substrates with a low or intermediate extraction ratio can accurately be scaled from adult clearance values down to children using a pediatric covariate function for CYP3A-mediated midazolam clearance. *This thesis*

5. Modelling approaches in the pediatric population that incorporate both drug-specific and system-specific properties, lead to more physiological knowledge in neonates, infants, and children. *Barret JS et al. Clin Pharmacol Ther. 2012*

6. The impact of intestinal metabolic extraction on bioavailability is often neglected. *Yang J et al. Curr Drug Metab. 2007*

7. A PKPD model is useful only when it can be used to answer a (clinical) question. *Standing JF, Br J Clin Pharmacol. 2017*

8. Mechanistic models taking into account developmental changes affecting absorption and (presystemic) clearance in children can optimize pediatric drug development. *Edginton AN, Paediatr Anaesth. 2011*


10. Those who have knowledge, do not predict; those who predict, lack knowledge or data. *Lao Tzo*

11. Less pressure to publish and inspiring role models in science lead to better research quality.

12. Working hard is important, but something else is even more important: believing in yourself.