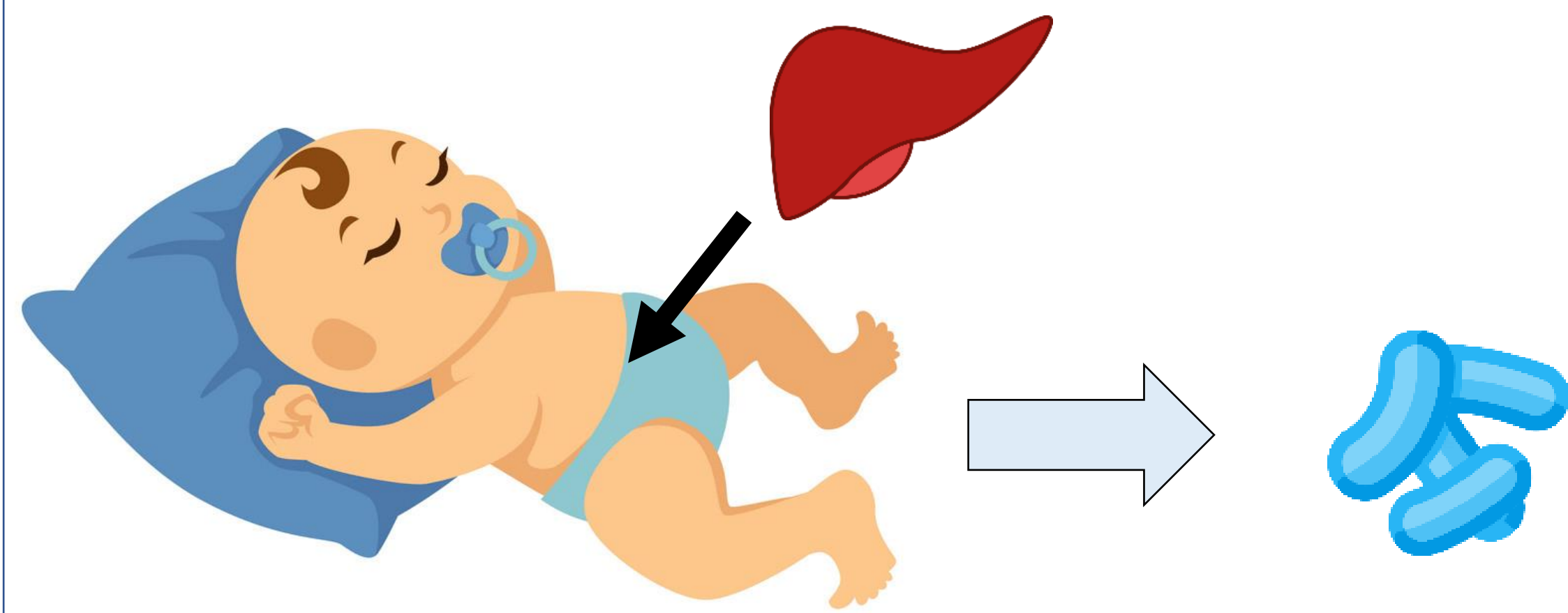


# Population pharmacokinetics and dosing simulation of the $\beta$ -lactam temocillin in liver-transplanted paediatric patients

Perrin Ngougni Pokem<sup>1,6</sup>, Xavier Stéphenne<sup>2</sup>, Dimitri Van der Linden<sup>3</sup>, Marie-Laura Godet<sup>2</sup>, Gert-Jan Wijnant<sup>1\*</sup>, Olga Chatzis<sup>3</sup>, Laurent Houtekie<sup>4</sup>, Astrid Haenecour<sup>4</sup>, Pierre Wallemacq<sup>5</sup>, Paul M. Tulkens<sup>1</sup>, Etienne Sokal<sup>2</sup>, Laure Elens<sup>6</sup>, Françoise Van Bambeke<sup>1</sup>

1. Pharmacologie cellulaire et moléculaire, Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium, 2. Pediatric Gastroenterology and Hepatology, Department of Paediatrics, Cliniques Universitaires Saint-Luc, Brussels, Belgium, 3. Pediatric Infectious Diseases, Department of Paediatrics, Cliniques Universitaires Saint-Luc, Brussels, Belgium, 4. Pediatric Intensive Care Unit, Department of Intensive Care, Cliniques Universitaires Saint Luc, Université Catholique de Louvain, Brussels, Belgium, 5. Clinical Chemistry Department, Cliniques Universitaires St. Luc, Université catholique de Louvain, Brussels, Belgium, 6. Integrated PharmacoMetrics, PharmacoGenomics and PharmacoKinetics, Louvain Drug Research Institute, Université catholique de Louvain, Brussels, Belgium.

## Introduction

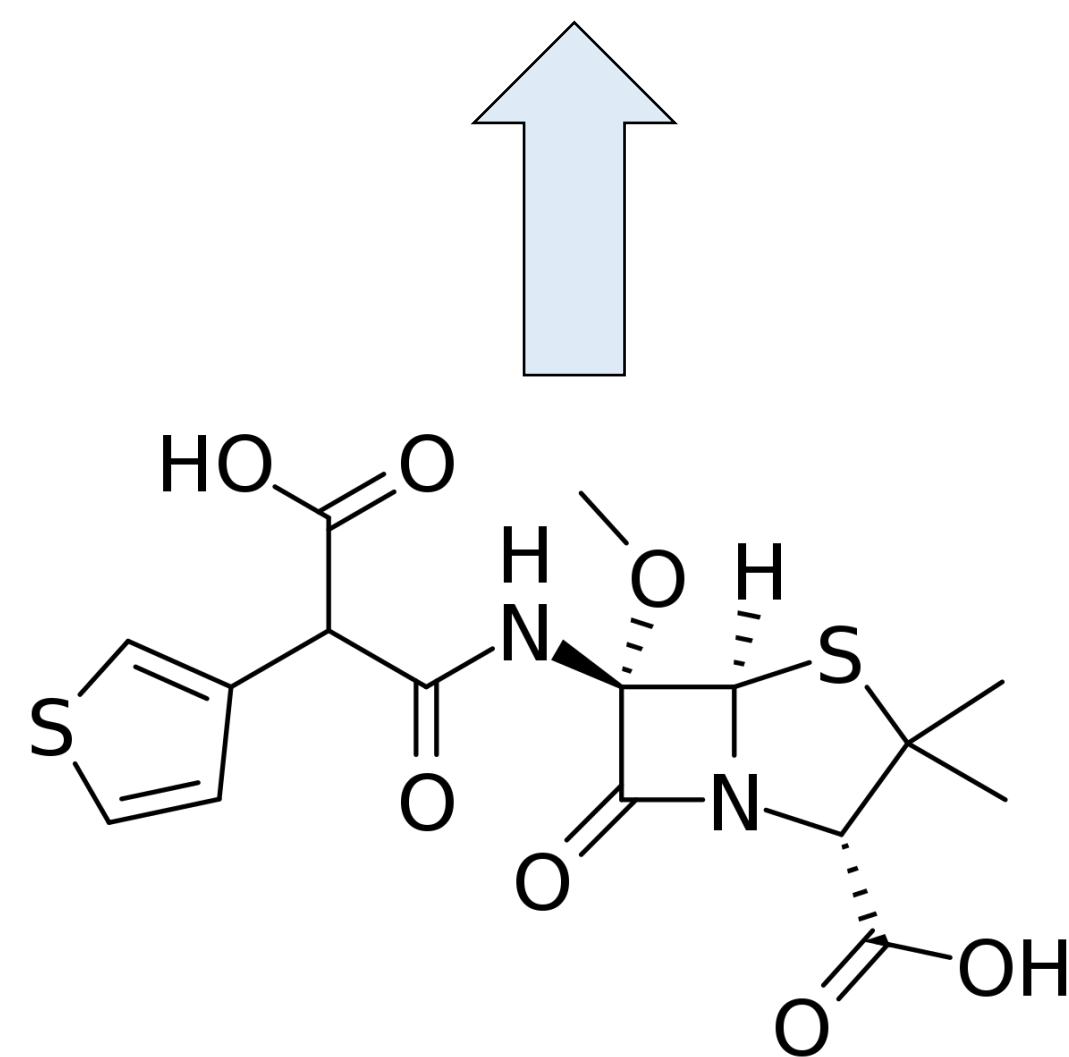


6-36-month-old requiring hepatic transplant

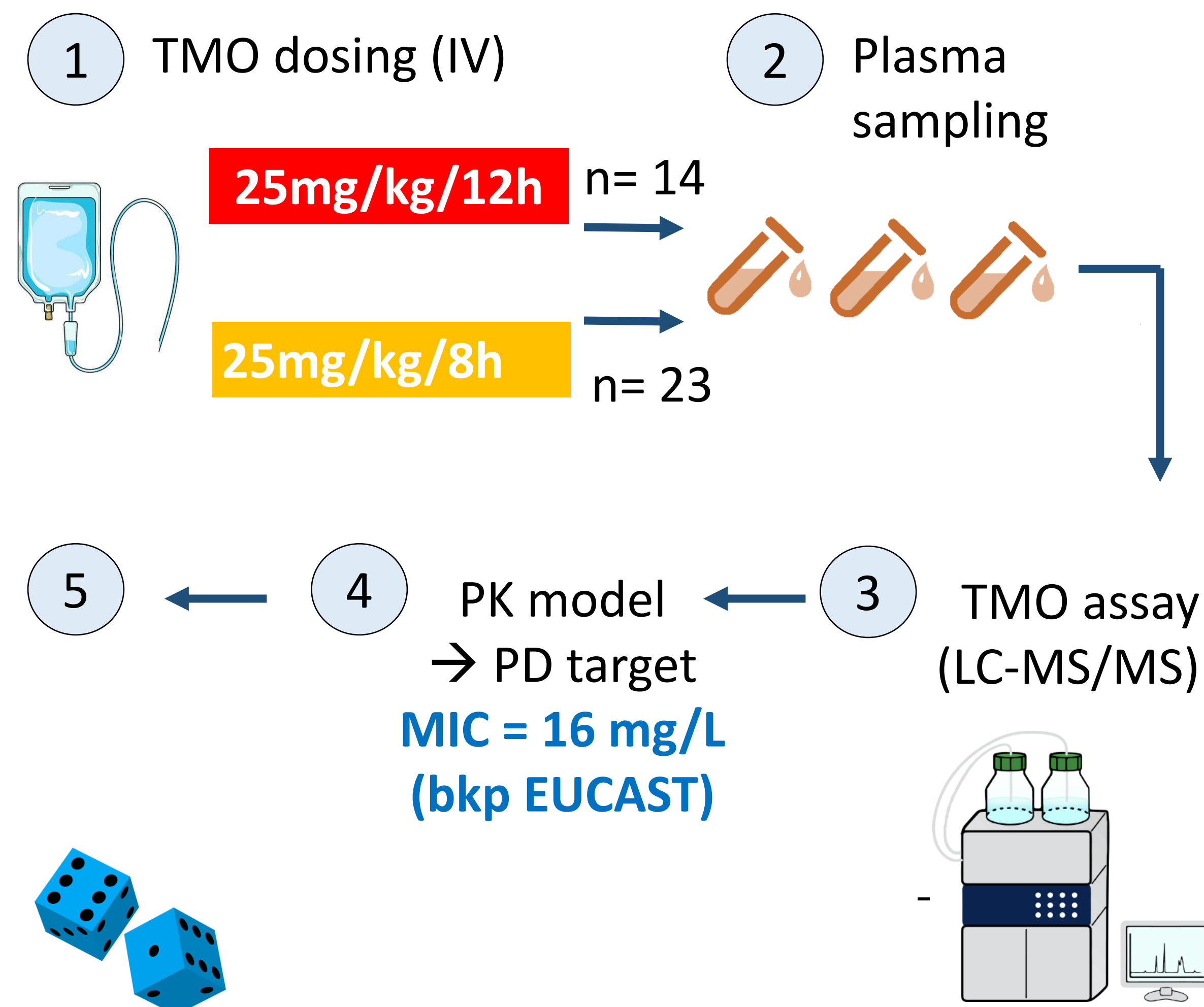
Immunosuppressants  
→ high risk infections  
→ (ESBL) Enterobacterales

### Temocillin (TMO)

- Carbapenem-sparing  $\beta$ -lactam antibiotic
- Dosing children (SPC):  
✓ Min = 25 mg/kg/12h  
✓ Max = 2g/12h
- So, what is the optimal dose for these patients?



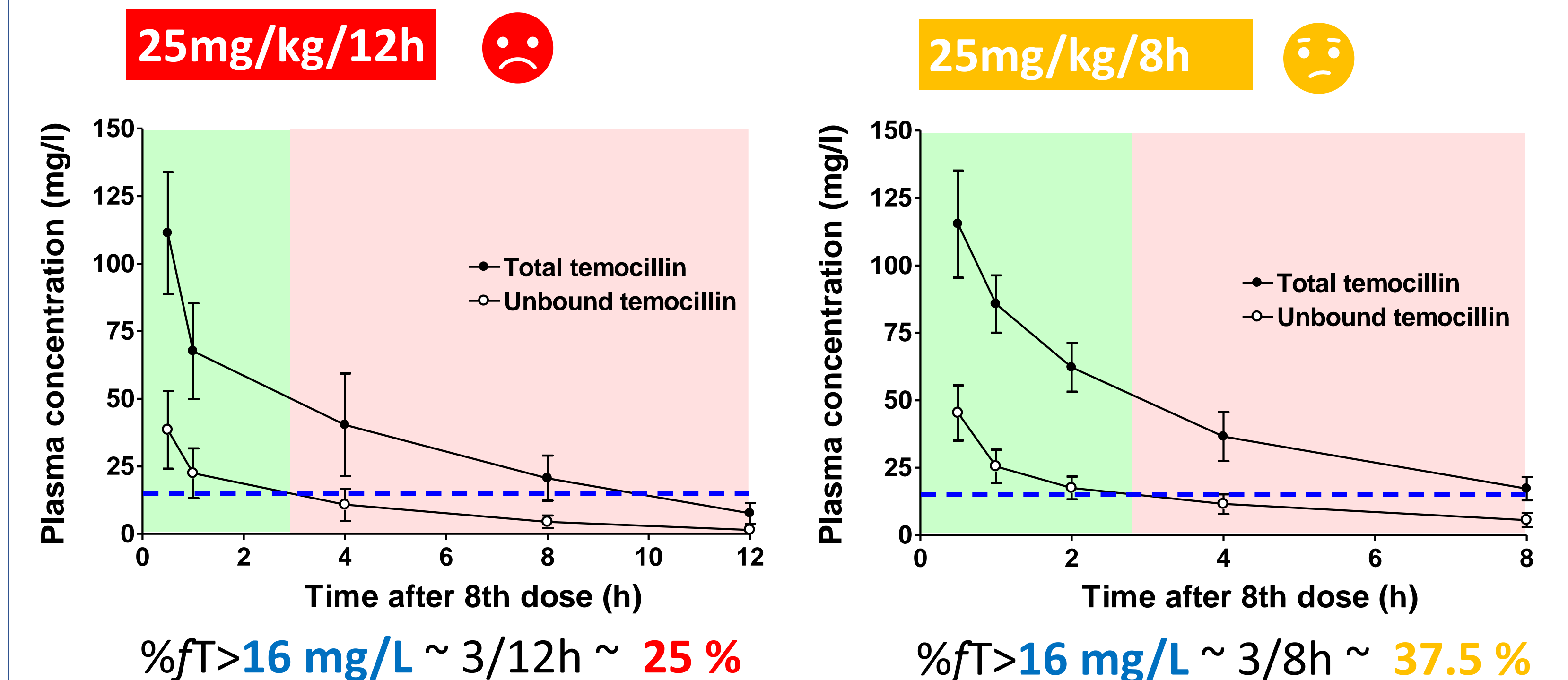
## Methodology



- Monte Carlo (n=1000)
- **Dosing simulations:** Probability of Target Attainment (PTA) ~ 40% fT>MIC

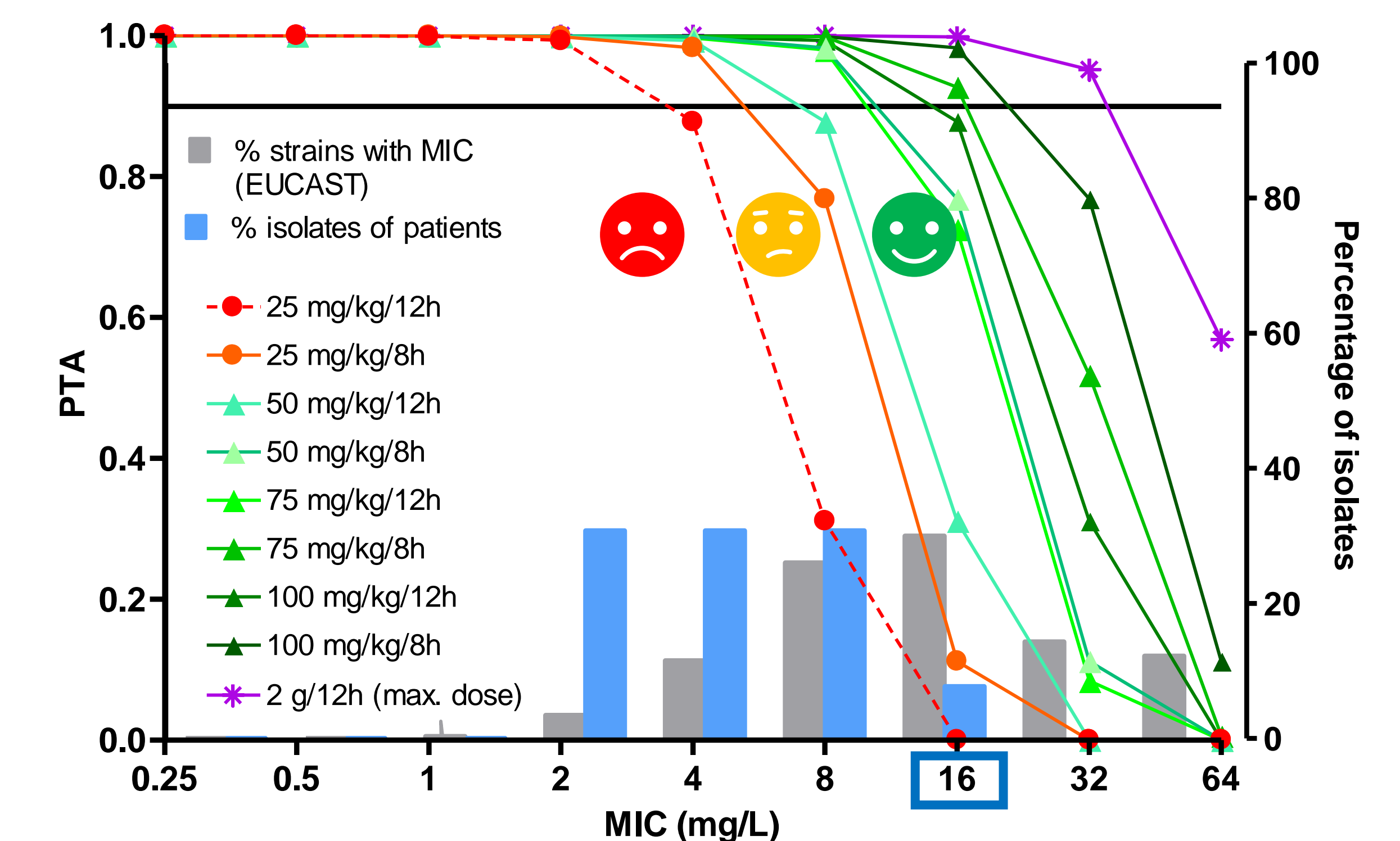
## Results

Clinically tested TMO doses: are they high enough?



2-compartmental PK model: renal function & body weight key co-variates

**Dosing simulations (higher, off-label doses):** PTA for  $\neq$  MICs?  
Data for typical patient: GFR = 139 mL/min & weight = 9.8 kg



## Conclusion: temocillin dosing in liver-transplanted children

- **25 mg/kg/12h** = SPC dose ~ risk underdosing!
- **25 mg/kg/8h** = new routine dose at Saint-Luc (better PK/PD, no safety concerns observed)
- **75 mg/kg/8h** = 90% PTA for majority of study population, but clinical safety = ???

### Risk factors underdosing at SPC dose

