SIMULATIONS OF VANCOMYCIN EXPOSURE TROUGHOUT CHILDHOOD UPON COMMONLY USED DOSING GUIDELINES: TOWARDS A MODEL-BASED DOSING GUIDELINE

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Background

- Daily practice: target concentrations of vancomycin are hard to reach
- Recently a GFR model for vancomycin was described in children [1]

Objectives

- Evaluation of vancomycin exposure in children upon several dosing regimens
- Development of a model-based dosing regimen

Methods

- Simulation of concentrations-time profiles for ten representative children on the basis of:

$$CL_i = CL_p \times \left(\frac{cBW}{4000g}\right)^k \qquad k = 2.23 \times cBW^{-0.065}$$

$$V_{central,i} = V_{central,p} \times \left(\frac{cBW}{4000g}\right)^1 \qquad Q = Cl;\ V_{peripheral} = V_{central}$$

- Simulated dosing guidelines:
  - Kinderformularium
  - BNFc
  - IDSA
- Targets:
  - C_{trough} (intermittent dosing): 10-15 mg/L
  - C_{ss} (continuous dosing): 15-25 mg/L
  - AUC_{24h}/MIC>400

Proposed model-based dosing regimen

Table 1. Proposed model-based dosing regimen for children aged > 1 month

	Current weight	Dosing guideline
Proposal-intermittent dosing	< 2.5 kg	32 mg/kg/day in 4 doses
	2.5-5.0 kg	40 mg/kg/day in 4 doses
	5.0-10.0 kg	52 mg/kg/day in 4 doses
	> 10 kg	60 mg/kg/day in 4 doses
Proposal-continuous dosing	< 2.5 kg	35 mg/kg/day
	2.5-5.0 kg	45 mg/kg/day
	5.0-10.0 kg	55 mg/kg/day
	> 10 kg	60 mg/kg/day

Results

- Steady state concentrations were reached between 31 and 53 hours for respectively children aged >1 year and a 1 month old child

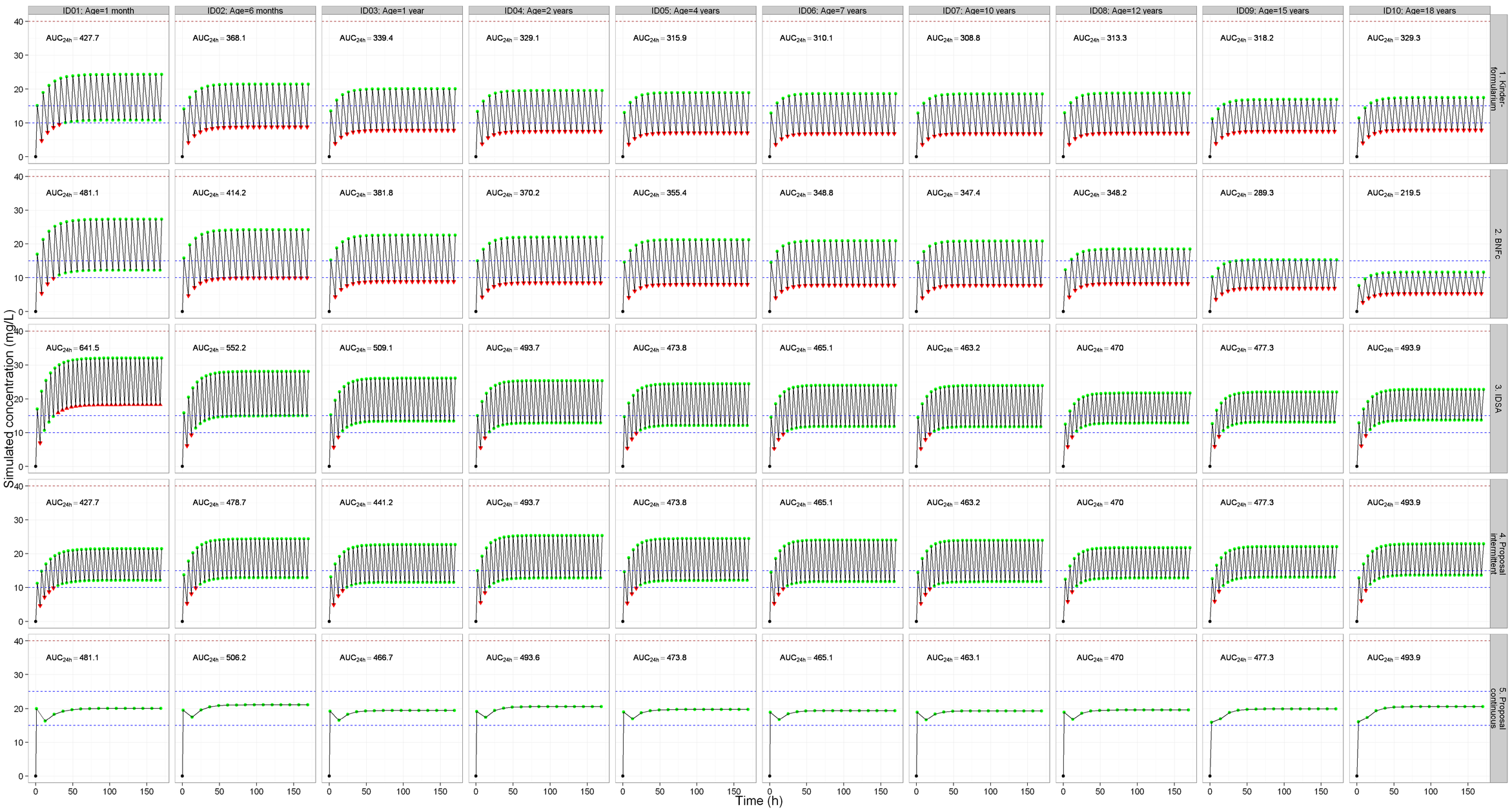

Figure 1. Comparison of currently used and proposed vancomycin dosing regimens for ten representative children with age 1 month-18 years
ID1: 1 month, cBW=3.5 kg; ID2: 6 months, cBW=6 kg; ID3: 1 year, cBW=9 kg; ID4: 2 years, cBW=11 kg; ID5: 4 years, cBW=16 kg; ID6: 7 years, cBW=22 kg; ID7: 10 years, cBW=30 kg; ID8: 12 years, cBW=45 kg; ID9: 15 years, cBW=55 kg; ID10: 18 years, cBW=75 kg
- - - - - - : target range for trough concentration (intermittent dosing; 10-15 mg/L) or Css concentration (continuous dosing; 15-25 mg/L)
- - - - - - : concentrations above this line (40 mg/L) may lead to toxicity
AUC_{24h}: AUC on the last 24 h of treatment
● : concentration is within the target range or peak concentration is not exceeding 40 mg/L
▼ : concentration is below the target range
▲ : concentration is above the target range

Discussion

- The proposed dosing algorithm leads to comparable vancomycin exposure in children with age varying between 1 month and 18 years

References

[1] De Cock RFW *et al*, Pharm Res 2014

Conflicts of interests: none

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