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Assessment of glomerular filtration rate by population pharmacokinetics of iohexol in children and young adults with cancer and infection

Hiie Soeorg[1], Aveli Noortoots[2], Jana Lass[3], Kadri Saks[4], Maarja Karu[4], Irja Lutsar[1], Lenne-Triin Kõrgvee[5]

[1]University of Tartu, Department of Microbiology, Tartu, Estonia,[2]University of Tartu, Institute of Clinical Medicine, Tartu, Estonia, [3]Tartu University Hospital, Pharmacy, Tartu, Estonia, [4]Tallinn Children's Hospital, Department of Haematology and Oncology, Tallinn, Estonia, [5]Tartu University Hospital, Hematology-Oncology Clinic, Tartu, Estonia

Conflict of Interest

X	No, Nothing to disclose
	Yes, please specify

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Background

Children with cancer and infection may develop **augmented renal clearance**

Sub-therapeutic concentrations of antibiotics

Therapeutic failure

Adjustment in dosing

Correct assessment of renal function

- Most widely used creatinine-based eGFR equations imprecise
- Cystatin C-based eGFR could perform better
- Exogenous (e.g. iohexol) markers are preferred

eGFR – estimated glomerular filtration rate

Aim

- We aimed to
  - describe renal function by measured GFR using **iohexol clearance** and
  - assess the predictive performance of **creatinine- and cystatin C-based eGFR** equations

in children and young adults with cancer and infection.

(e)GFR – (estimated) glomerular filtration rate

Methods

Hospitalised patients aged **0.5-25 years**
- with suspected/confirmed **infection** receiving piperacillin-tazobactam or cefepime
- **eGFR ≥70 mL/min/1.73 m²** according to Schwartz (children, <19 years) or MDRD or CKD-EPI equation (adults, ≥19 years)

↓

Iohexol administered within 24 h up to 6 d after start of treatment with antibiotics

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Iohexol concentrations measured prior to, 5 min, 0.5, 3-3.5, 5.5-8 h after administration

↓

Iohexol concentration data described by **population pharmacokinetic model** in NONMEM

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GFR=clearance (L/h)/60*1000/(body surface area (m²)) x 1.73

↓

GFR and eGFR compared in terms of **bias** and **accuracy**

Creatinine and **cystatin C** measured 3 h later

↓

eGFR calculated by 21 most common equations

(e)GFR – (estimated) glomerular filtration rate

Children and young adults

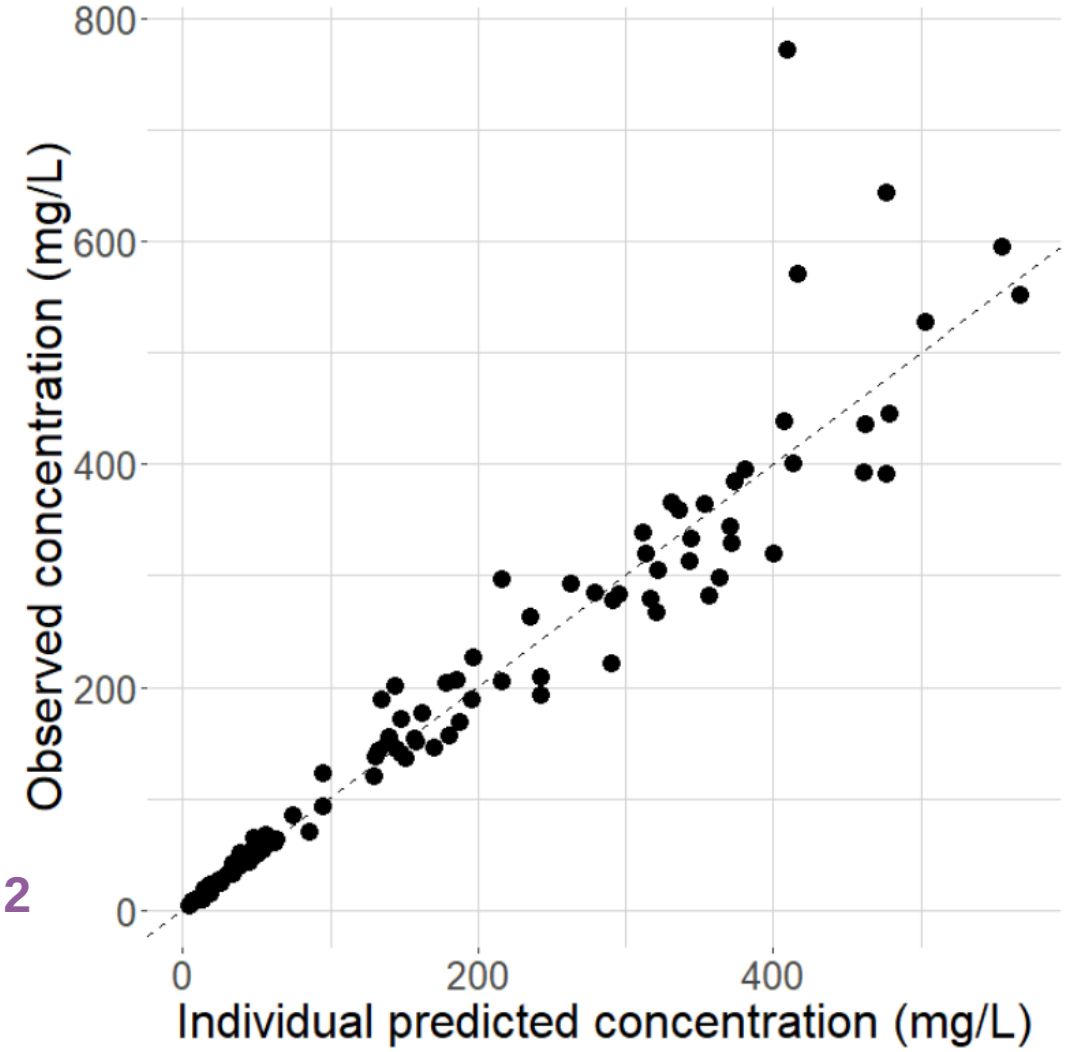
	Children (<19 years) (n=23)	Adults (≥19 years) (n=9)
Age (years) – median (range)	10 (0.7…17)	23 (20…25)
Male – n (%)	11 (47.8)	6 (66.7)
Body mass index z-score -2 to 2 – n (%)	18 (78%)	
Body mass index (kg/m^2) – median (range)		24.9 (17.9-33.3)
eGFR (mL/min/1.73 m^2)* – median (range)	148 (74 …234)	135 (105…177)

*eGFR value of 914 mL/min/1.73 m^2 in one child excluded as outlier.

eGFR – estimated glomerular filtration rate

Iohexol population pharmacokinetic model

- Three-compartment model:
  CL=6.50×(**weight**/70)$^{0.75}$×**e**$^{\eta}$,
  V=6.53×(**weight**/70),
  Q_{p1}=13.5,
  V_{p1}=8.33×(**weight**/70),
  Q_{p2}=0.72,
  V_{p2}=10.2
- Median (range) GFR was
  98 (68-138) mL/min/1.73 m²
  in children (<19 years) and
  112 (70-140) mL/min/1.73 m²
  in adults (≥19 years).



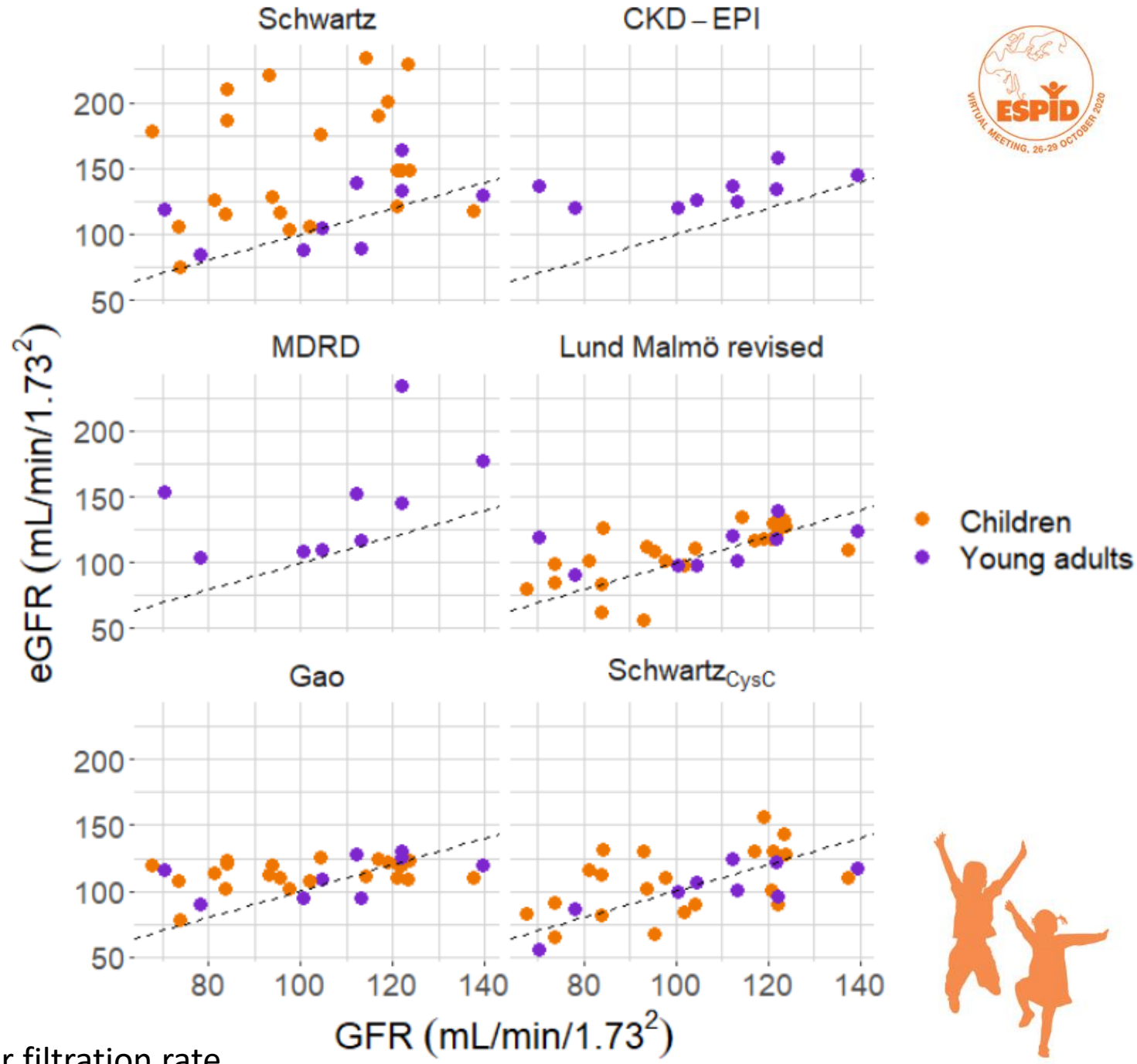
GFR – glomerular filtration rate

eGFR vs GFR

- All eGFR equations **overestimated** GFR and were **inaccurate**.

Equation	Bias (mL/min/1.73 m²)	P10 (%)
Schwartz	-27	26
CKD-EPI	-21	22
MDRD	-26	33
Lund Malmö revised	**-3**	**48**
Gao	-6	45
$Schwartz_{CysC}$	-4	23

Bias = median GFR-eGFR
P10 = percentage of eGFR within ±10% of GFR



(e)GFR – (estimated) glomerular filtration rate

Conclusions

- In children and young adults with cancer and infection creatinine- and cystatin C-based eGFR equations
  - overestimate GFR and
  - are with poor precision and accuracy.

- Adjustment of doses of renally eliminated antibiotics may need more reliable renal function measurements than creatinine- and cystatin C-based eGFR equations.

(e)GFR – (estimated) glomerular filtration rate

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