

# Factors influencing vancomycin dose adjustment at the Tartu University Hospital level 3 intensive care units

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**TDM** – therapeutic drug monitoring  
**PK** – pharmacokinetic  
**VAN** – Vancomycin  
**AUC<sub>24</sub>**– Area under the serum concentration vs. time curve for 0-24 hours  
**TUH** – Tartu University Hospital  
**Ctrough** – trough concentration (target range 10-20 mg/L)

# Background

## Vancomycin (VAN)

High interindividual PK variability  
Narrow therapeutic range



**TDM recommended**

## VAN dosing in TUH

- eGFR > 50 ml/min → 1000mg x2
- eGFR < 50 ml/min → 1000mg x1 + Ctrough TDM

### Trough-only based TDM

- Target 10 to 20 mg/L
- No guideline for dose adjustments
- ↑ nephrotoxicity
  - Targeting ~~15-20~~ mg/L

### AUC<sub>24</sub>-based TDM

- Target 400 to 600 µg/mL x h
- Preferred model-informed precision dosing  
→ Optimised dosing scheme

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# Aim

**To determine factors influencing VAN dose adjustment following VAN Ctrough measurement.**

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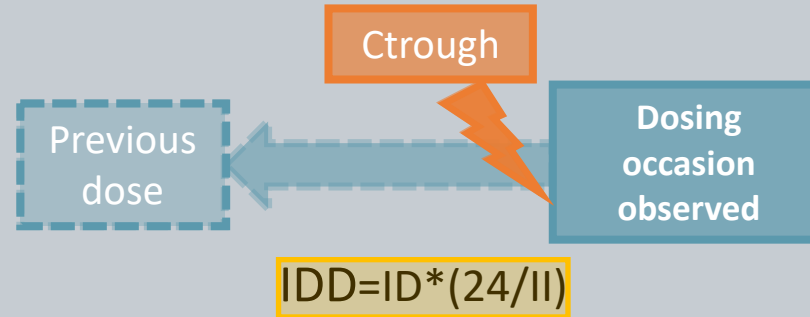
# Methods

## Population:

- $\geq 18$  years old
- Hospitalised to 3rd level ICU in TUH
- Receiving i/v VAN
- Measured at least 1 concentration
- 03.2020 to 03.2022

## Retrospective data collection

## Dosing occasions included



## The Classification and Regression Tree Analysis (CART)

- 56 different covariates
  - Previously published PK models
  - Literature research

## COVARIATES:

- **Patients' demographics:** age, sex, weight
- **Patient's comorbidities:** diabetes, liver function markers
- **Patient's condition:** invasive ventilation, dialysis, scores
- **Infection status:** Confirmed presence of G+ infection, location of presumed infection, CRP, WBC
- **Fluid status:** weight change, urine output
- **PK profile:** UREA, CRETININE, renal function estimation

**TDM** – therapeutic drug monitoring  
**ICU** – intensive care unit  
**PK** – pharmacokinetic  
**VAN** – Vancomycin  
**AUC<sub>24</sub>** – Area under the serum concentration vs. time curve for 0-24 hours  
**TUH** – Tartu University Hospital  
**Ctrough** – trough concentration (target range 10-20 mg/L)  
**IDD** – intended daily dose  
**ID** – intended dose  
**II** – intended interval

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**VAN** – Vancomycin  
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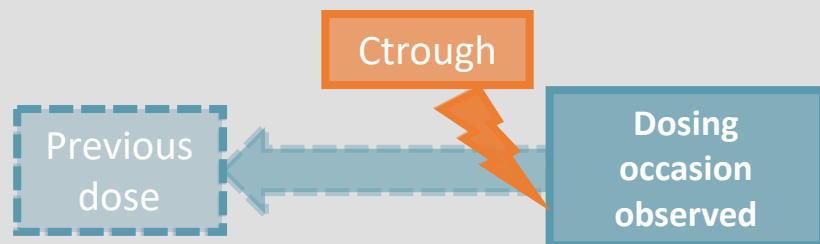
# Results

## 145 VAN treatment episodes:

- 133 different patients
- 2785 doses administered
- 1077 concentrations defined as Ctrough (67.5%)



**1052 dosing episodes suitable for CART**



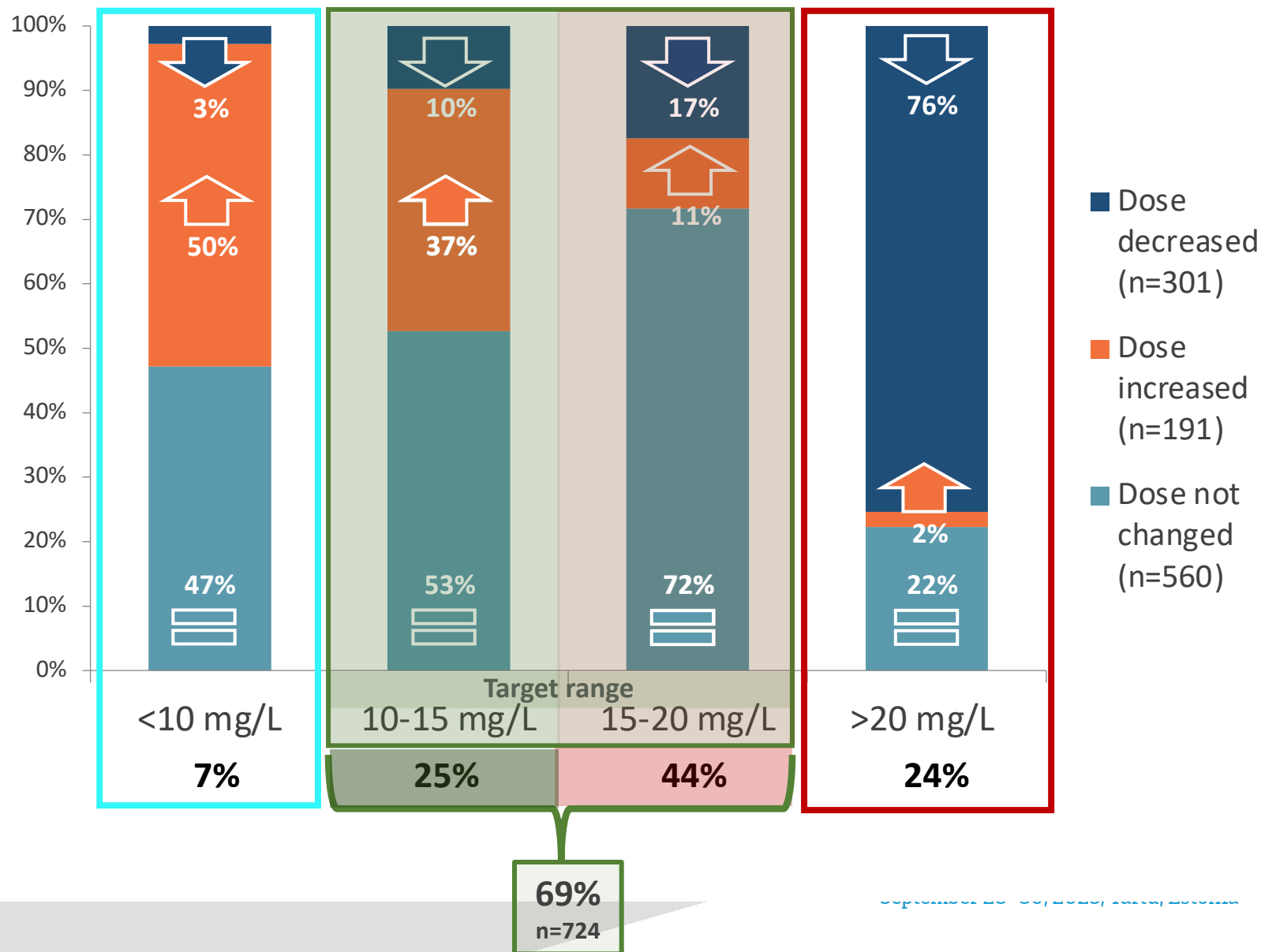
Parameter	Median (IQR)
<b>Male</b>	77.3%
<b>Age (years)</b>	63 (55-70)
<b>BMI (kg/m<sup>2</sup>)</b>	27.7 (24-31.3)
<b>Invasive ventilation</b>	60.7%
<b>VAN treatment duration (d)</b>	8 (5-12)
<b>eGFR (ml/min; n=1032)</b>	96.9 (66.3-109.1)
<b>Dialysis</b>	21.4%
<b>Doses per patient (n)</b>	5 (3-10)
<b>Daily dose (mg)</b>	1000 (1000-2000)
<b>Ctrough (mg/L)</b>	17.2 (14-19.9)

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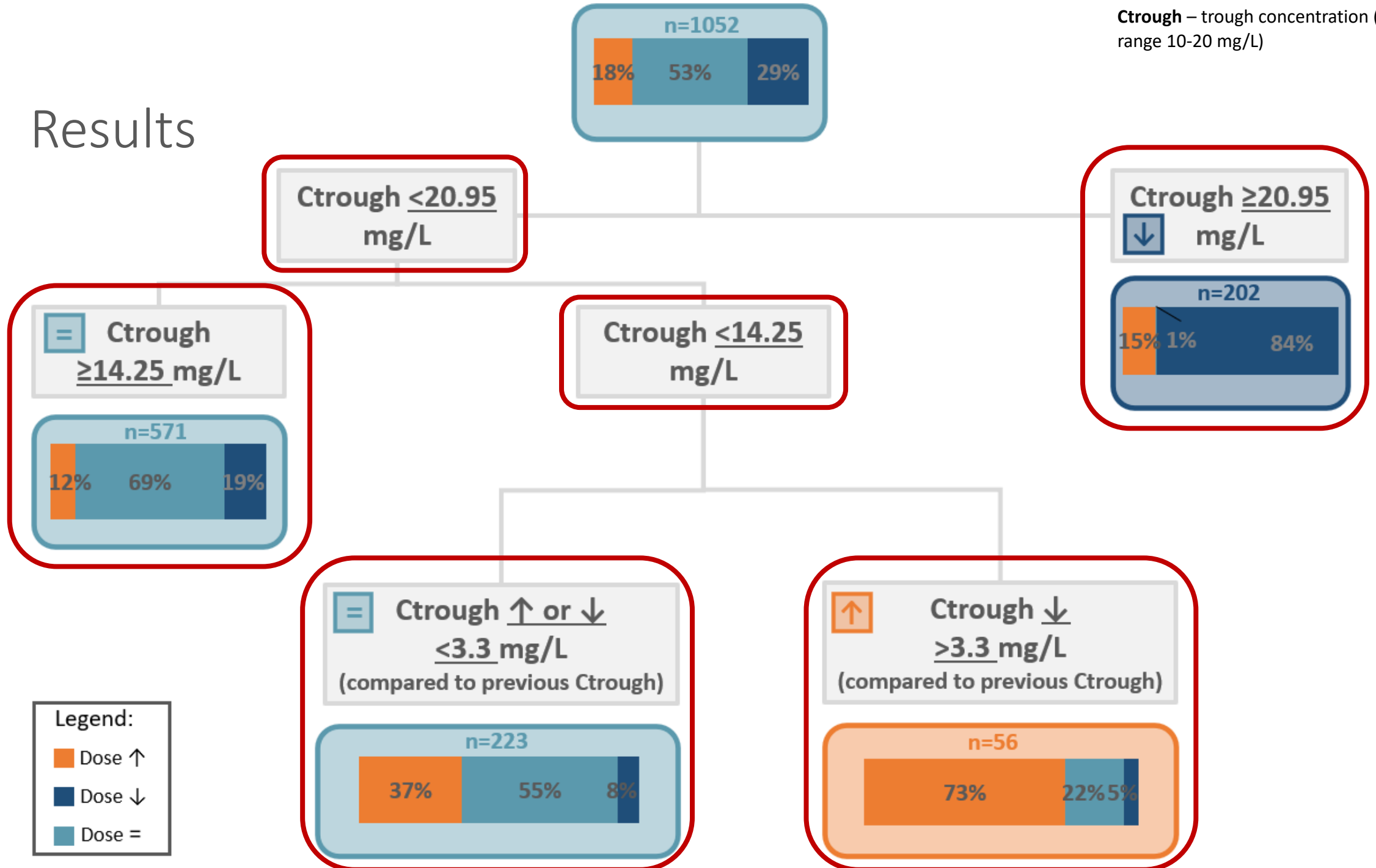
# Results

## Dose changes in relation to Ctrough values (n=1052)



Ctrough – trough concentration (target range 10-20 mg/L)

# Results



**VAN** – Vancomycin  
**TDM** – therapeutic target monitoring  
**Ctrough** – trough concentration (target range 10-20 mg/L)  
**AUC<sub>24</sub>**– Area under the serum concentration vs. time curve for 0-24 hours

# Summary

- Patient characteristics have little or no effect on dosing decisions
- VAN dosing is adjusted according to Ctrough-based TDM considering dynamics
- Higher Ctrough range is targeted 15-20 mg/L

## Recommendation to revising current TDM methodology

Lowering target range (10-15 mg/L)

OR

Upgrading to AUC<sub>24</sub>-based TDM



**Model-informed precision dosing**

Easier to use

↑ accurate

↓ nephrotoxicity

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# Thank you!

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**Tartu University Hospital  
intensive care units**

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