

Background

- Pharmacokinetic studies suggested that total body weight (TBW) could be the optimal approach for dosing intravenous vancomycin (15-20 mg/kg TBW every 8-12 h) for target achievement ($C_{ss} > 15$ mg/L). ⁽¹⁾
- However, recent data concluded that the use of adjusted body weight (ABW) might be a better approach in obese patients ($BMI \geq 30$ kg/m²). ⁽²⁾

Aim

To determine which is the preferred method **TBW, IBW or ABW** to optimize vancomycin therapy in obese patients.

Methods

- Retrospective, non-interventional, observational study.

Inclusion criteria

>18 years-old

Body mass index (BMI) ≥ 30 kg/m²

Creatinine clearance ≥ 60 mL/min

Therapeutic drug monitoring (TDM) at steady-state (SS)

- Non-obese patients were included as a control group.
- Vancomycin (VAN) **theoretically** total daily doses (15–20 mg/kg) were calculated using TBW, IBW and ABW for each patient (Theor-dose).

- We estimated TDM-doses by **Bayesian forecasting** (PKS® AbbotSoftware; target: $C_{ss} > 15$ mg/L) (TDM-dose).

- Theor*dose – *TDM*dose was calculated for each patient.

- Hypothetical** % of patients being over/underdosed using TBW/IBW/ABW and 15-20mg/kg were assessed.

- For each dosing-weight approach, the median of dose differences for over/underdosed patients, were calculated and were compared by each other.

- Dose differences higher than 10-12.5% between median doses were considered unsuitable, since they could be related to clinical failure or toxicity. Wilcoxon's test analysis was performed using SPSS® ($p < 0.05$).

Results

- 40 obese and 38 control patients were included. Higher CL and Vd values at SS were observed in obese patients compared to the control group. (Table 1)
- Results of number of over/underdosed patients, median and minimum/maximum dose differences in **obese group** for each dosing approach are shown in Table 2.

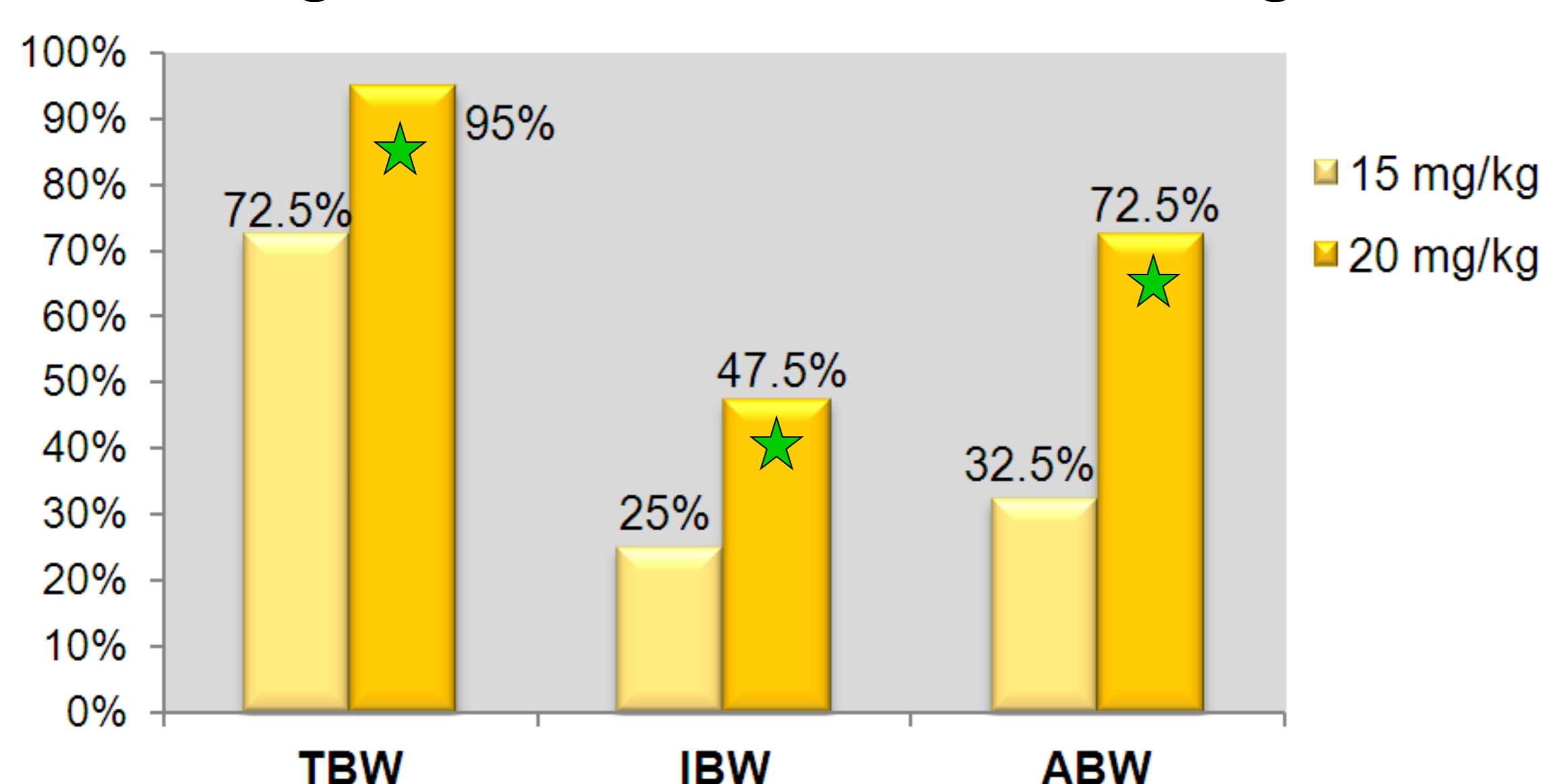
Table 2	TBW*		IBW*		ABW*	
VAN 15 mg/Kg	n		n		n	
Overdose	29	680 mg [50-2550]	10	236 mg [2-997]	13	358 mg [87-1385]
Underdose	9	-180 mg [(-10)-(-1050)]	30	-808 mg [(-79)-(-2166)]	27	-597 mg [(-18)-(-1887)]
Identical PK dose	2		0		0	
VAN 20 mg/Kg	n		n		n	
Overdose	38	1380 mg [200-3650]	19	500 mg [75-1579]	29	612 mg [22-2097]
Underdose	2	-150 mg [(-150)-(-150)]	18	-443 mg [(-99)-(-1639)]	11	-292 mg [(-29)-(-1266)]
Identical PK dose	0		3		0	

*median [min-max]

Table1	OBESE	CONTROL
Demographic data (mean \pm SD)		
Men	35%	61.5%
Age (years)	60.4 \pm 12.6	56.0 \pm 16.6
Weight (kg)	91.4 \pm 11.5	67.1 \pm 14.2
BMI (kg/m ²)	33.3 \pm 2.7	23.2 \pm 3.2
CICr (ml/min)	78.7 \pm 15.5	93.7 \pm 28.4
Population parameters (mean \pm SD)		
Vd ss (L/Kg)	58.0 \pm 11.8	48.2 \pm 13.0
Cl (L/h)	5.9 \pm 2.2	4.9 \pm 1.7
Predicted concentrations (mean \pm SD)		
Cmin ss (mg/L)	9.5 \pm 1.9	10.6 \pm 2.6
Cmax ss (mg/L)	24.7 \pm 4.3	26.9 \pm 4.3
Css (mg/L)	17.6 \pm 2.3	19.7 \pm 2.8

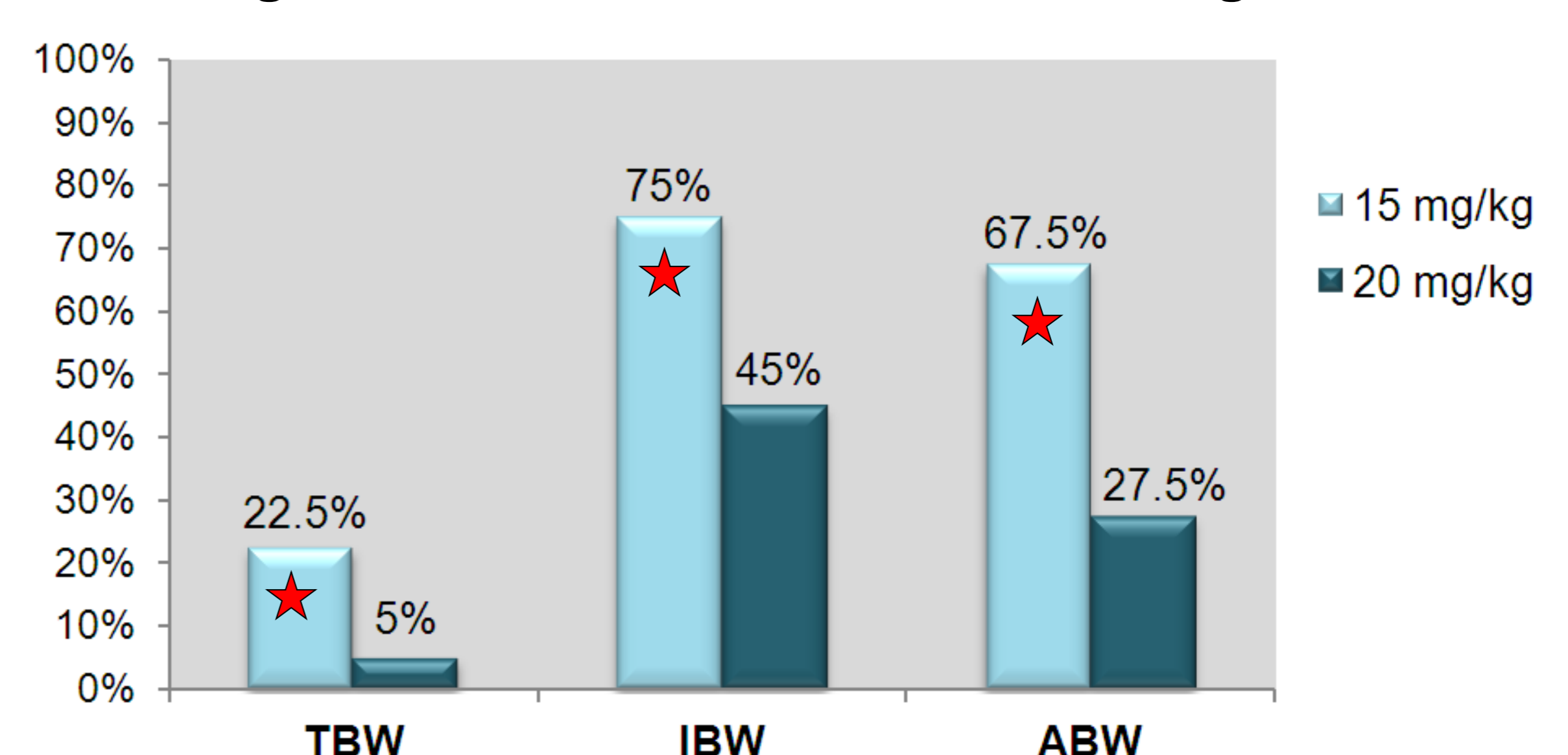
- In **obese patients**, results demonstrated a high frequency of VAN overdose when it was based on the TBW. It was lower for ABW. (Fig. 1) High frequency of underdosage was seen with IBW. It was also lower for ABW. (Fig. 2)

Fig. 1: Percentage of VAN overdose in OP according to TBW, IBW, ABW.



Statistically significant differences were seen (green stars) in 20 mg/kg group with median dose differences between TBW and IBW or ABW > 500 mg.

Fig. 2: Percentage of VAN underdose in OP according to TBW, IBW, ABW.



Statistically significant differences were seen (red stars) in 15 mg/kg group with median dose differences between TBW and IBW or ABW > 400 mg.

- In contrast, no relevant differences were observed in the **control group** by using TBW, ABW and IBW.

Conclusions

- Compared to the TDM-dose (optimal dose to achieve $C_{ss} > 15$ mg/L), **vancomycin overdose was highly observed in obese patients** ($BMI \geq 30$ kg/m²) by using TBW.
- IBW** resulted to be the worst approach because it could be related with an increased **risk of underdosage**.
- In our **obese patient** cohort, **ABW was the best approach** for dosing intravenous vancomycin, and hence, **vancomycin dosage: 15-20mg/ABW** kg might be recommended in obese patients.