2009 Complex *S. aureus* infections recommended vancomycin trough concentrations 15-20 mg/L

AUC$_{24}$/MIC > 400
Fig. 2. Scatter and linear fit plot of vancomycin area under the curve over 24 h (AUC24) versus trough vancomycin concentration from 5000 subject Monte Carlo simulation.
### Vancomycin-Induced Nephrotoxicity

In the “15-20 mg/L” Trough Era: A Systematic Review and Meta-Analysis

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Troughs &gt; 15 mg/L</th>
<th>Troughs &lt; 15 mg/L</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bosso et al (3)</td>
<td>42 142</td>
<td>13 146</td>
<td>4.30 [2.19, 8.43]</td>
</tr>
<tr>
<td>Cano et al (4)</td>
<td>22 89</td>
<td>7 99</td>
<td>4.32 [1.74, 10.69]</td>
</tr>
<tr>
<td>Chung et al (7)</td>
<td>12 25</td>
<td>16 48</td>
<td>1.65 [0.69, 4.96]</td>
</tr>
<tr>
<td>Hermansen et al (19)</td>
<td>5 16</td>
<td>4 39</td>
<td>3.98 [0.91, 17.46]</td>
</tr>
<tr>
<td>Hidayat et al (20)</td>
<td>11 63</td>
<td>0 32</td>
<td>14.24 [0.81, 249.87]</td>
</tr>
<tr>
<td>Jeffers et al (24)</td>
<td>27 49</td>
<td>13 45</td>
<td>3.02 [1.28, 7.11]</td>
</tr>
<tr>
<td>Kralovicova et al (26)</td>
<td>21 60</td>
<td>23 138</td>
<td>2.02 [1.04, 3.96]</td>
</tr>
<tr>
<td>Kumar et al (27)</td>
<td>27 139</td>
<td>23 141</td>
<td>1.24 [0.67, 2.29]</td>
</tr>
<tr>
<td>Kulic et al (28)</td>
<td>8 116</td>
<td>1 84</td>
<td>6.15 [0.75, 50.13]</td>
</tr>
<tr>
<td>Lodise et al (36)</td>
<td>7 27</td>
<td>14 139</td>
<td>3.13 [1.12, 8.69]</td>
</tr>
<tr>
<td>McKarns et al (38)</td>
<td>16 57</td>
<td>8 110</td>
<td>4.98 [1.98, 12.52]</td>
</tr>
<tr>
<td>Minejima et al (40)</td>
<td>17 72</td>
<td>25 155</td>
<td>1.61 [0.80, 3.21]</td>
</tr>
<tr>
<td>Prabaker et al (49)</td>
<td>7 54</td>
<td>24 294</td>
<td>1.68 [0.68, 4.11]</td>
</tr>
<tr>
<td>Zimmerman et al (63)</td>
<td>8 12</td>
<td>0 33</td>
<td>126.56 [6.19, 2585.90]</td>
</tr>
</tbody>
</table>

**Total (95% CI):**
- Troughs > 15 mg/L: 921 [150.00, 1.503]
- Troughs < 15 mg/L: 150.00 [1.503, 1.000]

**Heterogeneity:**
- $\chi^2 = 23.80, df = 13$ (P = 0.03), I² = 45%

**Test for overall effect:**
- $Z = 5.66 (P < 0.000001)$

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Vancomycin dosing

**Serious MRSA** infection an individualized target $\text{AUC}_{24}/\text{MIC}$ ratio of 400 to 600 mg.h/L (assuming a vancomycin MIC of 1 mg/L)

Vancomycin AUC monitoring also recommended

- all patients at high risk for nephrotoxicity (e.g., critically ill patients receiving concurrent nephrotoxins),
- patients with unstable (i.e., deteriorating or significantly improving) renal function,
- those receiving prolonged courses of therapy (>3 to 5 days).
New GGC Vancomycin dose guidelines will result in median

- Trough concentration 17 mg/L,
- $C_{av\ ss}$ of 24 mg/L
- $AUC_{24}$ 576 mg.h/L
Update (and validate) vancomycin dose calculator
  - Using adjusted body weight (or IBW) to calculate CrCl
Need to update gentamicin Dose calculator
Need to update CrCl dose calculator
Education

NEW GGC VANCOMYCIN DOSING GUIDELINES
Fig. 1. Probability of achieving an AUC/MIC ratio \( \geq 400 \) for vancomycin dosing regimens of varying intensity when trough vancomycin concentrations are between 15 and 20 mg/L.
MIC values (from ECOSS) based on MSSA bacteraemias

- MIC < 0.5 mg/L  40%
  - AUC/MIC ratio highly likely to be >400
  - AUC calculation **not** required
- MIC = 1 mg/L  59%
- MIC > 1 mg/L  1%
  - AUC/MIC ratio unlikely to be >400
  - Do **not** use vancomycin in these patients

VANCOMYCIN MIC'S
35-54 patients per day on vancomycin

Impossible to calculate AUC\textsubscript{24} in every vancomycin patient

Approx. 20 MRSA bacteraemia patients per year

In 2019 427 SAB patients

- Includes 20 MRSA
- 10\% penicillin allergy - 40 patients
- Based on MICs 60\% of these = 24 patients

“Do able” for AMPs to calculate AUC in 44 patients/year???
Vancomycin AUC monitoring also recommended

- all patients at high risk for nephrotoxicity (e.g., critically ill patients receiving concurrent nephrotoxins),
- patients with unstable (i.e., deteriorating or significantly improving) renal function,
- those receiving prolonged courses of therapy (>3 to 5 days).
HOW TO CALCULATE AUC\textsubscript{24}? 

- **Insight Rx**
  - 
- **GGC OPT**
  - Bayesian statistics
  - Calculates ofCss average (x24)
- **Elsewhere**
  - Online dose calculators
  - Use excel to work out AUC
GGC Antimicrobial pharmacists will calculate AUC 24 in MRSA/MSSA bacteraemia patients with vancomycin MIC = 1mg/L
THANK YOU

- Alison Thomson, Christine Pender, Fiona Robb, Karen Downie, Kimberley Philip, Lee Stewart, Mairi MacLeod, Michael Da Silva Neto, Rachael Rodger, Susan Kafka