Definitions and Equations

\[ \text{BMI} = \frac{\text{weight (kg)}}{\text{height}^2 (\text{m}^2)} \]

<table>
<thead>
<tr>
<th>WHO BMI Classification</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obese Class I and II (obese)</td>
<td>BMI 30-40 kg/m²</td>
</tr>
<tr>
<td>Obese Class III (morbidly obese)</td>
<td>BMI ≥ 40 kg/m²</td>
</tr>
</tbody>
</table>

### Body Weight

<table>
<thead>
<tr>
<th>IBW (kg)</th>
<th>Equation¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: 50.0 + 2.3 × (number of inches over 5 ft)</td>
<td></td>
</tr>
<tr>
<td>Female: 45.5 + 2.3 × (number of inches over 5 ft)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ABW (kg)</th>
<th>IBW + C × (TBW – IBW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C = either 0.3 or 0.4 (ABW₅₆, or ABW₇₆)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>LBW₂₀₀₅ (kg)</th>
<th>Equation²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male: ( \frac{9270 \times TBW}{6680 + 216 \times \text{BMI}} )</td>
<td></td>
</tr>
<tr>
<td>Female: ( \frac{9270 \times TBW}{8780 + 244 \times \text{BMI}} )</td>
<td></td>
</tr>
</tbody>
</table>

**LBW (for anti-tuberculosis medications):**
- Lean Body Weight (men) = \( (1.10 \times \text{Weight(kg)}) - 128 \times (\text{Weight}^2/(100 \times \text{Height(m)})^2) \)
- Lean Body Weight (women) = \( (1.07 \times \text{Weight(kg)}) - 148 \times (\text{Weight}^2/(100 \times \text{Height(m)})^2) \)

### Table 1.³ Recommended Antibiotic Dosing in Obesity (BMI ≥ 30 kg/m²)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum Dose^a</th>
<th>Study Type^b</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-lactams</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>No Data</td>
<td></td>
<td>- Consider upper limit of normal dosing in severe infections, e.g. up to 1g PO TID</td>
</tr>
<tr>
<td>Ampicillin</td>
<td>Insufficient data</td>
<td></td>
<td>- Consider upper limit of normal dosing in severe infections, e.g. up to 2g q4h</td>
</tr>
<tr>
<td>Nafcillin</td>
<td>Insufficient data</td>
<td></td>
<td>- Single case report in critically ill, obese patient: consider upper end of normal dosing in severe infections, e.g. up to 2 g q4h</td>
</tr>
<tr>
<td>Piperacillin-</td>
<td>Up to 4.5 g q8h (prolonged infused over 4 hours) or 4.5 g q6h (30 min infusion)</td>
<td></td>
<td>- Prolonged infusions preferred for critically ill, obese patients</td>
</tr>
<tr>
<td>tazobactam14</td>
<td></td>
<td></td>
<td>- High dose, prolonged infusion if critically ill, obese, with CrCl &gt; 100 ml/min</td>
</tr>
<tr>
<td>Cefazolin15-21</td>
<td>Insufficient data</td>
<td></td>
<td>- Consider upper limit of normal dosing in severe infections, e.g. up to 2 g q8h (option for continuous infusion)²², or 1.5-2 g q6h intermittent dosing</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>No data</td>
<td></td>
<td>- Consider upper end of normal dosing in severe infections, e.g. 500-1000 mg q6h</td>
</tr>
<tr>
<td>Cefepine,</td>
<td>Up to 2g q8h prolonged infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ceftazidime14,24,25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Ceftazidime/avibactam
- No change

### Ceftolozane/tazobactam
- No change

### Doripenem
- No change
- Consider extended infusion if targeting a higher PD endpoint of 100% fT>MIC or with less susceptible pathogens (i.e. MIC > 2)

### Ertapenem
- No change

### Imipenem
- No data
- Use caution in renal impairment and with high doses (1g q6h): increased risk of seizures

### Meropenem
- Same dose: consider prolonged infusion for critically ill patients
- Prolonged infusion if critically ill, obese with CrCl > 100 ml/min, if targeting a higher PD endpoint of 100% fT>MIC, or infections with less susceptible pathogens (i.e. MIC > 2)

### Monobactam
- Insufficient data
- Single case report suggests higher dosing needed
- Consider upper end of normal dosing in severe infections, e.g. 2g q6-8h

### Fluoroquinolones

#### Ciprofloxacin
- In critically ill, septic patients on CRRT with organisms with MICs > 0.5mg/L (e.g. P. aeruginosa, A. baumannii): > 90kg: 400 mg IV q8h
- Insufficient data except as noted in critically ill, septic patients on CRRT.
- Consider upper end of normal dosing in severe infections, e.g. up to 400 mg IV q8h or 750mg PO BID

#### Levofloxacin
- 750 mg q24h
- PK reportedly unaltered by obesity, however, serum levels may be sensitive to CrCl: 1,000 mg q24h has been suggested for CrCl IBW > 110 ml/min to target gram negative pathogens

#### Moxifloxacin
- No change

### Aminoglycosides

#### Amikacin
- Use adjusted body weight (ABW_{0.4}) for initial dose
- Adjust by TDM

#### Gentamicin
- Use adjusted body weight (ABW_{0.4}) for initial dose
- Adjust by TDM

#### Tobramycin
- Use adjusted body weight (ABW_{0.4}) for initial dose
- Adjust by TDM

### Polymyxins

#### Colistin methanesulfonate
- Use IBW
- Maximum dose of 360 mg daily to limit the risk of nephrotoxicity

#### Polymyxin B
- Limited data. Consider adjusted body weight (ABW_{0.4}), especially in upper end of dosing range
- Consider maximum dose 200 mg or 2 million units daily to limit risk of toxicity

### Anti-MRSA agents

#### Ceftaroline
- No change

#### Clindamycin
- IV: 600 mg q6h or 900 mg q8h
- PO: 450 - 600 mg q6h or 600- 900 mg Q8H
- Studies from prosthetic joint infection and SSTI suggest increased doses warranted
- Manufacturer maximum: 2,700 mg/day in severe infections; 4,800 mg/day given by intermittent or continuous infusion for life-threatening infections
<table>
<thead>
<tr>
<th>Drug</th>
<th>Notes/References</th>
<th>Dosing Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalbavancin</td>
<td>78-81</td>
<td>No change</td>
</tr>
<tr>
<td>Daptomycin</td>
<td>10,81,81-91</td>
<td>Same weight-based dose but use adjusted body weight (ABW&lt;sub&gt;0.4&lt;/sub&gt;)&lt;br&gt;- Caution in renal insufficiency, dialysis. Monitor CKs and signs of myopathy</td>
</tr>
<tr>
<td>Linezolid</td>
<td>18,37,81,92-100</td>
<td>No change&lt;br&gt;- Caution in renal insufficiency, dialysis. Monitor CKs and signs of myopathy</td>
</tr>
<tr>
<td>Oritavancin</td>
<td>81</td>
<td>No change</td>
</tr>
<tr>
<td>Sulfamethoxazole/trimethoprim</td>
<td>76,101</td>
<td>SSTI or severe/complicated UTI: up to 320 mg PO BID or 8-10 mg/kg&lt;sub&gt;ABW&lt;/sub&gt;/day in divided doses&lt;br&gt;- Limited data to guide optimal dosing weight&lt;br&gt;- Consider adjusted body weight when using high doses (e.g. &gt;8 mg/kg/day)</td>
</tr>
<tr>
<td>Tedizolid</td>
<td>81,102,103</td>
<td>No change</td>
</tr>
<tr>
<td>Telavancin</td>
<td>81,104,105</td>
<td>Same dose; consider a maximum of 1,000 mg/dose&lt;br&gt;- Increased systemic exposure may be related to AKI&lt;br&gt;- These are tentative pending results of an ongoing Phase I trial (NCT02753855)</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>81,82,108,109</td>
<td>No change</td>
</tr>
<tr>
<td>Vancomycin</td>
<td>18,37,61,108-192</td>
<td>See Vancomycin Per Pharmacy Protocol (Appendix C)&lt;br&gt;- Alternative approach using ABW&lt;sub&gt;0.4&lt;/sub&gt;: loading dose 25-30 mg/kg&lt;sub&gt;ABW&lt;/sub&gt;, initial maintenance dose approximately 15 mg/kg&lt;sub&gt;ABW&lt;/sub&gt; q12h*, then adjust by TDM&lt;br&gt;- Loading doses commonly ranged from none to 3g; daily doses commonly ranged 2-4g or 20-30 mg/kg&lt;sub&gt;TBW&lt;/sub&gt;/day&lt;br&gt;- Adjust doses by TDM (peak and trough) using software utilizing Bayesian methods and AUC targets.&lt;br&gt;- If calculating without software, see Hong et al for equations.&lt;br&gt;- If only measuring troughs, more cautious and frequent initial monitoring of levels may be warranted</td>
</tr>
</tbody>
</table>

a. Does not include dose adjustments for renal and/or hepatic impairment. Doses listed are within usual safety margins. Lower doses may be sufficient in mild infections (e.g. UTI). Dosages are based on the provided references and/or the authors' opinion, and should not replace clinical judgment. CrCl assumes calculation using ABW<sub>0.4</sub> unless specified in table.
b. Dots represent types of studies available and not quantity.
c. Dosing recommendations are for severe or deep-seated infections based on similarities in PK profile and dosing recommendations with other antibiotics of the same class when there is insufficient or no data in obese patients.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum Dose&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Study Type&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Case studies</td>
<td>PK/PD studies</td>
</tr>
</tbody>
</table>
| Caspofungin<sup>133-135</sup> | 70 mg x1, then 50-70 mg daily                 | ● ● ●      |               | - Retrospective study from 9 clinical studies found no significant difference in favorable responses in invasive candidiasis between obese and non-obese groups  
  - PK studies showed no correlation with BMI and PK parameters, but did find negative correlation between caspofungin peak levels and body weight, suggests increased doses needed for higher TBW  
  - In clinical trial of invasive candidemia, no safety concerns found with caspofungin 150mg daily                                          |
| Fluconazole<sup>135-139</sup> | Candidiasis: 12mg/kg x1 load, then 6mg/kg q24h (TBW) | ● ● ●      |               | - Doses up to 1200 mg daily have been reported in the literature for Cryptococcus meningitis  
  - In critically ill, esp with CrCl > 50, higher doses may be warranted to achieve PK/PD target of fAUC/MIC > 100, esp if MIC > 2 Candida spp  
  - Consider TDM for severe infections                                                                                           |
| Liposomal Amphotericin<sup>138</sup> | Use total or adjusted body weight              | ● ● ●      |               | - No PK data in obese humans; in general pop PK studies, linear increase in Vd and CL with weight  
  - Safety data: at doses 7.5-15mg/kg/day, similar discontinuation rates; PK became non-linear (max Cmax and AUC at 10mg/kg/day)  
  - Adjust dosing based on TDM                                                                                                      |
| Voriconazole<sup>,135,140-145</sup> | Use adjusted body weight or LBW<sub>2005</sub> | ● ● ●      |               | - Retrospective TDM studies frequently showed supratherapeutic levels in obese subjects when dosed by TBW  
  - Steady state plasma PK of voriconazole did not suggest weight-based dose adjustments necessary                                                                 |

<sup>a</sup> Maximum dose for obesity (BMI ≥ 30 kg/m<sup>2</sup>)

<sup>b</sup> Study type: Case studies, PK/PD studies, Clinical outcomes
Table 3. Recommended Antiviral Dosing in Obesity (BMI ≥ 30 kg/m²)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maximum Dose(^a)</th>
<th>Study Type(^b)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acyclovir(^{146-148})</td>
<td>Use ideal or adjusted body weight</td>
<td>PK/PD studies</td>
<td>- PK study: 5mg/kg IV x1 showed that dosing based on IBW in obese patients led to lower AUC than dosing by TBW in normal-weight patients. Authors suggest using ABW - Renal function may be a more important consideration than weight-based dosing in obese patients</td>
</tr>
<tr>
<td>Cidofovir(^{149})</td>
<td>Use adjusted body weight</td>
<td></td>
<td>- No data</td>
</tr>
<tr>
<td>Foscarnet(^{149})</td>
<td>Use adjusted body weight</td>
<td></td>
<td>- Based on similar PK profile and physicochemical properties as acyclovir, long intracellular half-life (except foscarnet, which deposits in bone), dose-limiting toxicity (e.g. myelosuppression)</td>
</tr>
</tbody>
</table>
References:


130. Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of
and comprehensiv