Superhero or Superzero?
Vancomycin vs. Linezolid for MRSA Pneumonia

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Western New England University

Disclosures

• BD and SH have nothing to disclose
Learning Objectives

1. Review appropriate use of MRSA-active agents in pneumonia
2. Compare the evidence for vancomycin and linezolid in MRSA pneumonia
3. Discuss potential implications of selecting a preferential agent for MRSA pneumonia

MRSA Coverage in Pneumonia

• 2016 IDSA/ATS HAP/VAP Guidelines recommend vancomycin or linezolid
  • Previous IV antibiotics within 90 days
  • Septic shock or ventilatory support required due to pneumonia
  • MRSA prevalence >10-20% in unit/institution
  • ARDS preceding VAP
  • Acute renal replacement therapy preceding VAP
• Recommended duration of 7 days
MRSA in Nosocomial Pneumonia

• *S. aureus* responsible for 31.9-36.5% of HAP/VAP in SENTRY surveillance program
  • ~50% were methicillin-resistant
• MRSA colonization
  • MRSA nasal swabs have 99% negative predictive value for MRSA pneumonia
  • Positive predictive value only around 37%

We Need YOUR Help!

Use the Kahoot! App or go to [www.kahoot.it](http://www.kahoot.it) to play along!

- Enter the Game PIN
- Choose a screen name
- Choose your superhero!
Here it comes to save the day: Mighty Vancomycin

<table>
<thead>
<tr>
<th></th>
<th>Rubinstein et al.</th>
<th>Wunderink et al.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Vancomycin</td>
<td>Linezolid</td>
</tr>
<tr>
<td>Clinical Cure</td>
<td>68.1%</td>
<td>66.4%</td>
</tr>
<tr>
<td>Microbiologic Cure</td>
<td>71.8%</td>
<td>67.9%</td>
</tr>
<tr>
<td>Adverse Events</td>
<td>33.7%</td>
<td>31.0%</td>
</tr>
<tr>
<td>Conclusion</td>
<td>Linezolid non-inferior to vancomycin</td>
<td>Linezolid non-inferior to vancomycin</td>
</tr>
</tbody>
</table>

Vancomycin vs. Linezolid Meta-analysis

- 9 randomized trials with direct comparison in nosocomial pneumonia
- Most used a fixed dose of vancomycin 1 g IV q12h
- Many did not allow monitoring and dose adjustment of vancomycin

**Meta-analysis – Clinical Cure**

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**Hospital-Acquired Pneumonia: Linezolid vs. Vancomycin: Clinical Response**

<table>
<thead>
<tr>
<th>Group by Study Design</th>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Mortality / Total</th>
<th>Risk difference and 90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Risk difference</td>
<td>Lower limit</td>
<td>Upper limit</td>
</tr>
<tr>
<td>RCT Double-blinded</td>
<td>Lublinen E 2005</td>
<td>-0.049</td>
<td>0.121</td>
<td>0.549</td>
</tr>
<tr>
<td>RCT Double-blinded</td>
<td>Vancuvin R 2003</td>
<td>-0.012</td>
<td>0.050</td>
<td>0.749</td>
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<tr>
<td>RCT Double-blinded</td>
<td>Jakob C 2000</td>
<td>-0.016</td>
<td>0.051</td>
<td>0.209</td>
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<tr>
<td>RCT Double-blinded</td>
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<td>-0.014</td>
<td>0.158</td>
<td>0.848</td>
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<tr>
<td>RCT Double-blinded</td>
<td>Vancuvin R 2012</td>
<td>0.012</td>
<td>0.050</td>
<td>0.749</td>
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<tr>
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<td>Vancuvin R 2012</td>
<td>0.017</td>
<td>0.154</td>
<td>0.305</td>
</tr>
<tr>
<td>RCT Open-label</td>
<td>Rever C 2002</td>
<td>0.005</td>
<td>0.141</td>
<td>0.159</td>
</tr>
<tr>
<td>RCT Open-label</td>
<td>Kappen S 2003</td>
<td>-0.011</td>
<td>0.151</td>
<td>0.241</td>
</tr>
<tr>
<td>RCT Open-label</td>
<td>Kohn S 2007</td>
<td>-0.006</td>
<td>0.106</td>
<td>0.360</td>
</tr>
<tr>
<td>RCT Open-label</td>
<td>Vancuvin R 2008</td>
<td>0.002</td>
<td>0.145</td>
<td>0.373</td>
</tr>
<tr>
<td>RCT Open-label</td>
<td>Vancuvin R 2008</td>
<td>-0.004</td>
<td>0.096</td>
<td>0.357</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>0.009</td>
<td>0.031</td>
<td>0.430</td>
</tr>
</tbody>
</table>

*Intention-to-Treat Population: Z=4.152; p=4.469; Heterogeneity: Q=6.378; P=0.661; I²=0%.

## Meta-analysis – Microbiologic Cure

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Study Name</th>
<th>Risk Difference</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>p Value</th>
<th>Micro Eradication / Total</th>
<th>Risk Difference and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized Double-blind</td>
<td>Rubinstein E 2001</td>
<td>-0.039</td>
<td>-0.223</td>
<td>0.150</td>
<td>0.565</td>
<td>36 / 53</td>
<td>28 / 39</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Wunderink R 2003</td>
<td>0.037</td>
<td>-0.065</td>
<td>0.242</td>
<td>0.273</td>
<td>47 / 76</td>
<td>42 / 79</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Lin D 2005</td>
<td>0.237</td>
<td>-0.018</td>
<td>0.492</td>
<td>0.068</td>
<td>17 / 22</td>
<td>15 / 28</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Wunderink R 2012</td>
<td>0.045</td>
<td>-0.095</td>
<td>0.183</td>
<td>0.537</td>
<td>35 / 97</td>
<td>26 / 82</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Siwek D 2002</td>
<td>0.062</td>
<td>-0.025</td>
<td>0.149</td>
<td>0.181</td>
<td>135 / 248</td>
<td>111 / 228</td>
</tr>
<tr>
<td>Randomized Open-label</td>
<td>Komo S 2007</td>
<td>0.000</td>
<td>-0.242</td>
<td>0.242</td>
<td>1.000</td>
<td>9 / 12</td>
<td>12 / 16</td>
</tr>
<tr>
<td>Randomized Open-label</td>
<td>Wunderink R 2005</td>
<td>0.092</td>
<td>-0.211</td>
<td>0.394</td>
<td>0.553</td>
<td>13 / 23</td>
<td>9 / 19</td>
</tr>
<tr>
<td>Randomized Open-label</td>
<td>0.020</td>
<td>-0.140</td>
<td>0.201</td>
<td>0.727</td>
<td>35 / 70</td>
<td>28 / 54</td>
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</tr>
<tr>
<td>Overall</td>
<td>0.056</td>
<td>-0.022</td>
<td>0.133</td>
<td>0.159</td>
<td>170 / 315</td>
<td>139 / 282</td>
<td></td>
</tr>
</tbody>
</table>

*Microbiologic Evaluable Per-Protocol Population, Z=1.406; P=0.159; Heterogeneity: G2=3.504; P=0.757; I2=40%.


## Meta-analysis – Mortality

<table>
<thead>
<tr>
<th>Study Design</th>
<th>Study Name</th>
<th>Risk Difference</th>
<th>Lower Limit</th>
<th>Upper Limit</th>
<th>p Value</th>
<th>Mortality / Total</th>
<th>Risk Difference and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized Double-blind</td>
<td>Rubinstein E 2001</td>
<td>-0.077</td>
<td>-0.157</td>
<td>0.004</td>
<td>0.363</td>
<td>36 / 200</td>
<td>49 / 192</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Wunderink R 2003</td>
<td>0.030</td>
<td>-0.086</td>
<td>0.183</td>
<td>0.363</td>
<td>64 / 331</td>
<td>61 / 202</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Jansen B 2006</td>
<td>0.018</td>
<td>-0.036</td>
<td>0.091</td>
<td>0.310</td>
<td>17 / 309</td>
<td>23 / 329</td>
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<tr>
<td>Randomized Double-blind</td>
<td>Lin D 2005</td>
<td>0.042</td>
<td>-0.013</td>
<td>0.118</td>
<td>0.553</td>
<td>13 / 71</td>
<td>21 / 71</td>
</tr>
<tr>
<td>Randomized Double-blind</td>
<td>Wunderink R 2012</td>
<td>0.011</td>
<td>-0.056</td>
<td>0.023</td>
<td>0.318</td>
<td>54 / 397</td>
<td>100 / 387</td>
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<tr>
<td>Randomized Double-blind</td>
<td>Siwek D 2002</td>
<td>0.051</td>
<td>-0.042</td>
<td>0.142</td>
<td>0.362</td>
<td>246 / 1606</td>
<td>236 / 1404</td>
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<tr>
<td>Randomized Open-label</td>
<td>Komo S 2007</td>
<td>0.031</td>
<td>-0.016</td>
<td>0.077</td>
<td>0.363</td>
<td>12 / 215</td>
<td>3 / 101</td>
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<tr>
<td>Randomized Open-label</td>
<td>Wunderink R 2005</td>
<td>0.020</td>
<td>-0.010</td>
<td>0.040</td>
<td>0.545</td>
<td>4 / 75</td>
<td>6 / 74</td>
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<tr>
<td>Randomized Open-label</td>
<td>0.019</td>
<td>-0.004</td>
<td>0.002</td>
<td>0.035</td>
<td>78 / 820</td>
<td>49 / 446</td>
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<tr>
<td>Overall</td>
<td>-0.006</td>
<td>-0.023</td>
<td>0.011</td>
<td>0.082</td>
<td>246 / 2528</td>
<td>236 / 1600</td>
<td></td>
</tr>
</tbody>
</table>

*Intention-to-Treat Population, Z=0.019; P=0.982; Heterogeneity: G2=1.651; P=0.232; I2=12.5%.


### Vancomycin vs. Linezolid for MRSA Pneumonia

**Hospital-Acquired Pneumonia: Linezolid vs. Vancomycin: Microbiological Eradication**

**Hospital-Acquired Pneumonia: Linezolid vs. Vancomycin: Mortality**
Problems with Linezolid

- Outbreaks of linezolid-resistant *S. aureus* have been reported
- Higher drug costs
- Drug interactions
- Adverse effects
- Bacteriostatic

Linezolid Adverse Effects

- Neurotoxicity
  - Peripheral neuropathy is potentially irreversible
- Serotonin syndrome
- Gastrointestinal symptoms
  - Higher incidence in linezolid group in the meta-analysis
- Thrombocytopenia
Vancomycin vs. Linezolid for MRSA Pneumonia

Meta-analysis – Thrombocytopenia


**Why Should Vancomycin Be Preferred?**

- Years of experience and still very little resistance
- Standard of care at most institutions
- Preserve activity of alternative agents
- Significantly lower drug cost
- Fewer drug interactions
- Potentially lower incidence of neurotoxicity and thrombocytopenia
Linezolid to the rescue!

Linezolid for Pneumonia

- Rubinstein, 2001
  - Linezolid versus vancomycin for nosocomial pneumonia
  - Clinical cure rates similar; 66.4 vs 68.1%, P= 0.79, 95% CI -14.9 to 11.3
- Wunderink, 2003
  - Continuation study for nosocomial pneumonia
  - Clinical cure rates similar for ITT; 52.7 vs 52.2%, P=NS, 95% CI -8.3 to 9.2
- Wunderick, 2003
  - Linezolid versus vancomycin for MRSA pneumonia (subset analysis)
  - Clinical cure rates favored linezolid; 59 vs 35.5%, P=0.01, 95% CI 1.3 to 8.3
ZEPHyR Trial

- Randomized, double blind, multi-center controlled trial
- Linezolid 600 mg IV q12H vs. Vancomycin 15 mg/kg q12H

- Improving on the past
  - Vancomycin monitoring
  - Reducing duration of empiric therapy

- Clinical and Microbiologic Outcomes

ZEPHyr Trial – Clinical Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Linezolid</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>PP at EOT</td>
<td>83.3%</td>
<td>69.9%</td>
</tr>
<tr>
<td>mITT at EOT</td>
<td>80.1%</td>
<td>67.8%</td>
</tr>
<tr>
<td>PP at EOS</td>
<td>57.6%</td>
<td>46.6%</td>
</tr>
<tr>
<td>mITT at EOS</td>
<td>54.8%</td>
<td>44.9%</td>
</tr>
</tbody>
</table>

95% CI 4.9 to 22.0  95% CI 4.0 to 20.7  95% CI 0.5 to 21.6  95% CI 0.1 to 19.8

P = 0.042
ZEPHyr Trial – Microbiologic Outcomes

<table>
<thead>
<tr>
<th>Patients with Respiratory Cultures</th>
<th>Linezolid</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>EOS</td>
<td>61.4</td>
<td>50</td>
</tr>
<tr>
<td>EOT</td>
<td>82.6</td>
<td>54.1</td>
</tr>
</tbody>
</table>

IMPACT-HAP

- Multi-center, retrospective, observational study of MRSA VAP
- Adult patients admitted to ICU with VAP were included
- Outcomes
  - Clinical success
  - Mortality
  - Adverse Events
IMPACT-HAP Outcomes

- Clinical Success
  - RR 1.24, P= 0.018, 95% CI 1.06 to 1.32
- Mortality
  - 9.9 vs 9.2%, P=1.00
- Adverse Events
  - Thrombocytopenia (P= NS)
  - Anemia (P= NS)
  - Nephrotoxicity (P= NS)

And a little more recent...

- Tong, 2016
  - Retrospective, cohort study comparing linezolid versus vancomycin for known or suspected MRSA pneumonia
  - Change in preferred agent from vancomycin to linezolid
  - Primary outcome was antimicrobial utilization
Tong, 2016

- Mortality outcome
  - 10% vs 19.5%, P = 0.046
- Hospital LOS (median days)
  - 10 vs 12, P = 0.318
- Thrombocytopenia
  - 5.3 vs 3.9%, P = 0.754
- Nephrotoxicity
  - 3.3% vs 8.9%, P = 0.098

- Mortality (Vancomycin vs Linezolid)
  - OR 1.52 95% CI 1.02 to 2.28, P = 0.04

*Linezolid Convenience*

- Bioavailability ~100%
- 600 mg PO/IV q12H
- Improved penetration

- Murine Pneumonia model
  - Assessed humanized ELF concentrations
  - Vancomycin AUC:MIC = 104
  - Linezolid AUC:MIC = 228
  - Tedizolid AUC:MIC = 222
Budget buster?

- Incidence is low
- Cost is decreasing
- Tong, 2016
  - Total hospital charges no different

**Hospital Charges for MRSA Pneumonia**

<table>
<thead>
<tr>
<th></th>
<th>Linezolid</th>
<th>Vancomycin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Hospital Charges ($)</td>
<td>25900</td>
<td>32100</td>
</tr>
</tbody>
</table>


Vancomycin Returns
ZEPHyr Trial – Patients

- 1184 patients randomized (ITT population)
  - 484 (41%) had confirmed MRSA pneumonia (mITT population)
  - 339 (28%) included in per-protocol analysis
- Vancomycin patients had higher rates of:
  - Mechanical ventilation – 73.9% vs 66.9% (p=0.15)
  - Bacteremia – 10.8% vs 5.2% (p=0.039)
  - Kidney disease – 36.9% vs 27.9% (p=0.07)

ZEPHyr Trial – Outcomes

- Vancomycin levels were not optimized
  - Median on day 3 was 12.3 mg/L (IQR 7.6-17 mg/L)
  - Median on day 6 was 14.7 mg/L (IQR 9.5-19.9 mg/L)
- Pfizer had the ability to override clinical outcome decisions
- No differences in 60-day mortality
  - 15.7% for linezolid and 17.0% for vancomycin in ITT analysis
  - 28.1% for linezolid and 26.3% for vancomycin in mITT analysis
IMPACT-HAP

- Average vancomycin concentration at day 3 was 13 mg/L
- All isolates in the vancomycin arm had a vancomycin MIC >1
  - 72% with an MIC of 1.5
  - 28% with an MIC of 2

<table>
<thead>
<tr>
<th></th>
<th>Linezolid</th>
<th>Vancomycin</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28-day mortality</td>
<td>9.9%</td>
<td>9.2%</td>
<td>1.00</td>
</tr>
<tr>
<td>Days on mechanical ventilation</td>
<td>11</td>
<td>13</td>
<td>0.276</td>
</tr>
<tr>
<td>ICU length of stay</td>
<td>11</td>
<td>13</td>
<td>0.823</td>
</tr>
<tr>
<td>Hospital length of stay</td>
<td>18</td>
<td>16</td>
<td>0.773</td>
</tr>
</tbody>
</table>

Tong

- Difference in all-cause mortality, BUT:
  - This was a secondary endpoint
  - No data on vancomycin MICs or levels
  - No attempt to differentiate infection-related from other causes of mortality
  - Linezolid use increased at a greater rate than vancomycin use decreased
Vancomycin Monitoring

- AUC monitoring is going to be the new standard
- Continuous infusion vancomycin
  - Fewer levels required for monitoring
  - Less nephrotoxicity than intermittent infusion with similar outcomes

Linezolid Monitoring?

- Significant inter- and intra-patient variability in linezolid exposure
  - Optimal AUC was not achieved in 63% of patients
  - Optimal T>MIC was not achieved in 50% of patients
- Strong correlation between renal clearance and linezolid clearance ($r=0.933$, $p<0.001$)
  - Renal dysfunction associated with elevated serum concentrations
  - Elevated serum concentrations associated with thrombocytopenia

Linezolid: The Sequel

Vancomycin Dosing

• **What vancomycin dose should I give my patient?**

  • Vancomycin: 15 mg/kg q12H or Vancomycin 1000mg IV q12H
    • Not so fast!

• **I’m aiming for what vancomycin concentration? (And when do I get it?)**

  • Trough Concentration 15 – 20 mg/L
    • Not so fast!

Equations – Empiric Vancomycin Dosing

- Estimate CrCl
- Estimate Vanc clearance
  - \( VCI = 0.8 \times (CrCl \times 0.06) \)
- Estimate Vd
  - Critically III/ESRD/fluid overloaded- 0.7-0.75L/kg
  - Obese- 0.5-0.6L/kg
  - Normal- 0.65-0.7L/kg
- Estimate Ke (\( Ke = Cl/Vd \)) (Eq#1)
  - Or: \( Ke = (0.00083 \times CrCl) + 0.0044 \) (Eq#2)
- \( Eq#1 \) may be preferred when \( CrCl > 120 \)
- Determine half life
  - \( T_{1/2} = 0.693/Ke \)
- Determine dosing interval
  - \( Tau = 1.5 \times T_{1/2} \)
- Calculate Total Daily Dose (TDD)
  - \( TDD = VCl \times \) Desired AUC
- Goal \( AUC_{0-24,24-48} = 500-700 \)
- Goal \( AUC_{48} = 400-700 \)
- Calculate maintenance dose (MD)
  - \( MD = TDD/(24/Tau) \)
- Estimate Cmax
  - \( Cmax = \frac{MD/Tinf}{Ke \times Vd} \times \frac{(1-e^{-Ke(T_{inf})})}{(1-e^{-Ke(T_{tau})})} \)
- Estimate Cmin
  - \( Cmin = Cmax \times e^{-Ke(T_{tau}-T_{inf})} \)

“Two point” Kinetics

\[
Vd=\left(\frac{Dose[\text{mg}]}{T_{inf}}\right) \times \frac{1-e^{-KeT_{inf}}}{Ke \times (Cmax-(Cmin \times e^{-KeT_{inf}}))}
\]

\[
Cmax = C1/e^{-KeT} \quad \text{(Where T= time (hours) since the end of infusion to C1)}
\]

\[
Cmin = C2(e^{-KeT}) \quad \text{(Where T= time (hours) from C2 to the next dose)}
\]
Vancomycin Trough Concentrations

“Our data indicate that adjustment of vancomycin doses on the basis of trough concentrations without a Bayesian tool results in poor achievement of maximally safe and effective drug exposures in plasma and that many adults can have an adequate vancomycin AUC with a trough concentration of <15 mg/liter.”

Adverse Events

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>log(Odds Ratio)</th>
<th>SE</th>
<th>Total</th>
<th>Total</th>
<th>Weight</th>
<th>Odds Ratio IV, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anderson 2015 abstract (49)</td>
<td>0.9163</td>
<td>0.2644</td>
<td>202</td>
<td>253</td>
<td>9.6%</td>
<td>2.50 [1.49, 4.20]</td>
</tr>
<tr>
<td>Balasubramanian 2013 abstract (41)</td>
<td>3.2119</td>
<td>1.4447</td>
<td>90</td>
<td>45</td>
<td>0.9%</td>
<td>24.82 [1.46, 421.22]</td>
</tr>
<tr>
<td>Belo 2015 abstract (42)</td>
<td>1.3286</td>
<td>0.4163</td>
<td>63</td>
<td>70</td>
<td>6.5%</td>
<td>3.77 [1.67, 8.52]</td>
</tr>
<tr>
<td>Burgess 2014* (26)</td>
<td>0.9083</td>
<td>0.4872</td>
<td>92</td>
<td>99</td>
<td>5.4%</td>
<td>2.45 [0.95, 6.44]</td>
</tr>
<tr>
<td>Carrero 2015 abstract (44)</td>
<td>1.5754</td>
<td>0.5337</td>
<td>71</td>
<td>71</td>
<td>3.8%</td>
<td>4.02 [1.69, 13.78]</td>
</tr>
<tr>
<td>Chong 2015 abstract (45)</td>
<td>1.9824</td>
<td>1.2278</td>
<td>17</td>
<td>5</td>
<td>1.2%</td>
<td>7.73 [0.66, 81.36]</td>
</tr>
<tr>
<td>Fodero 2016* (27)</td>
<td>1.1663</td>
<td>0.4379</td>
<td>286</td>
<td>165</td>
<td>1.0%</td>
<td>3.21 [1.36, 7.57]</td>
</tr>
<tr>
<td>Garst 2014 abstract (48)</td>
<td>0.6293</td>
<td>0.2862</td>
<td>276</td>
<td>153</td>
<td>3.1%</td>
<td>1.88 [1.07, 3.29]</td>
</tr>
<tr>
<td>Hellwig 2011 abstract (49)</td>
<td>1.4691</td>
<td>0.3118</td>
<td>210</td>
<td>327</td>
<td>2.2%</td>
<td>4.43 [2.41, 8.17]</td>
</tr>
<tr>
<td>Katchan 2015 abstract (51)</td>
<td>0</td>
<td>0.6506</td>
<td>91</td>
<td>91</td>
<td>1.0%</td>
<td>1.00 [0.28, 3.58]</td>
</tr>
<tr>
<td>Kim 2015* (30)</td>
<td>1.772</td>
<td>0.6992</td>
<td>101</td>
<td>101</td>
<td>2.2%</td>
<td>5.88 [1.49, 23.16]</td>
</tr>
<tr>
<td>Meaney 2014* (32)</td>
<td>1.679</td>
<td>0.6629</td>
<td>58</td>
<td>36</td>
<td>4.4%</td>
<td>5.36 [1.41, 20.44]</td>
</tr>
<tr>
<td>Min 2011 abstract (52)</td>
<td>2.2817</td>
<td>0.4977</td>
<td>73</td>
<td>67</td>
<td>4.9%</td>
<td>3.89 [0.80, 25.73]</td>
</tr>
<tr>
<td>Norbury 2014 abstract (54)</td>
<td>2.3026</td>
<td>0.7683</td>
<td>86</td>
<td>25</td>
<td>4.2%</td>
<td>10.00 [2.22, 45.08]</td>
</tr>
<tr>
<td>Rutter 2017* (37)</td>
<td>0.708</td>
<td>0.081</td>
<td>5497</td>
<td>3055</td>
<td>3.0%</td>
<td>2.03 [1.73, 2.38]</td>
</tr>
<tr>
<td>Scully 2014 abstract (55)</td>
<td>1.6535</td>
<td>0.641</td>
<td>94</td>
<td>44</td>
<td>2.6%</td>
<td>5.23 [1.49, 18.35]</td>
</tr>
<tr>
<td>Sutton 2018 (39)</td>
<td>1.5624</td>
<td>0.4607</td>
<td>108</td>
<td>116</td>
<td>5.6%</td>
<td>4.92 [1.92, 12.61]</td>
</tr>
<tr>
<td>VanQuroph 2015 abstract (56)</td>
<td>1.0448</td>
<td>0.3926</td>
<td>160</td>
<td>100</td>
<td>4.9%</td>
<td>2.94 [1.32, 6.41]</td>
</tr>
</tbody>
</table>

Total (95% CI): 7517 4822 100.0% 3.40 [2.57, 4.59]
Vancomycin MIC

- Testing method is important
  - Automated susceptibility testing vs E-test vs broth microdilution

- Haque, 2010
  - Increase of 1 mg/L = Increased Mortality
  - Unadjusted OR 3.73 (95% CI 1.45 to 9.62)

- Choi, 2011
  - Early clinical response of low (≤ 1 mg/L) vs high (≥ 1.5 mg/L) vancomycin MIC
  - 63.9 vs 35.3% P=0.031

Linezolid just makes sense

- With appropriate antimicrobial stewardship, linezolid use should not create a budget crisis
  - Limit use to patients with risk factors
  - Implementation of MRSA nasal swabs
  - Appropriate durations of therapy
  - Quick and effective IV to PO switches to expedite transitions of care

- Vancomycin isn’t worth the time
  - Dosing has become too complicated
  - Adverse events can be significant
  - MICs (within the susceptible range) matter
Who is the Ultimate Pneumonia Superhero?

Use the Kahoot! App or go to www.kahoot.it to play along!

- Enter the Game PIN
- Choose a screen name
- Choose your superhero!

Questions?