Multivariate analysis of factors affecting *Clostridium difficile* infection rates; the more you look, the more you find; but should you believe what you see?

Longitudinal European *Clostridium difficile* Infection Diagnosis Surveillance Study (LuCID)

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Disclosures

• Received research funding:
  ▫ Astellas Pharma Europe Ltd
  ▫ bioMérieux
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• Received honorarium from:
  ▫ Astellas Pharma Europe Ltd
  ▫ Summit
Objectives

• To investigate variability in *C. difficile* testing and positivity according to place and time.

• To describe the profile of in-patients who have *C. difficile* infection (CDI) and the timing of the onset of the disease.

• Impact of testing policies on CDI rates
  ▫ *How* are samples tested for CDI?
  ▫ *Is* there seasonality of CDI?
Study design

Institution demographic data collection → Monthly testing data collection (April 2014-March 2015) → Analysis

France
Italy
UK
Spain
Germany


Definitions – testing methods

• Direct toxin detecting CDI testing algorithms (recommended)
  ▫ GDH or NAAT followed by toxin detection\(^1\)\(^-\)\(^3\)
  ▫ Defines ‘true’ CDI\(^1\)\(^-\)\(^3\)

• Other CDI testing methods
  ▫ Algorithm (not recommended)
    • An algorithm other than the ‘recommended’ algorithms
    • e.g. Toxin/culture or Toxin/NAAT
  ▫ Method ONLY detecting toxin
    • Stand-alone, direct toxin detection
    • e.g. single toxin enzyme immunoassay (EIA)
  ▫ Method NOT detecting toxin
    • Any method that does not detect toxin directly from the sample
    • e.g. NAAT

Hospital/laboratory descriptions
Small = <100,000 pbd/annum
Medium = 100,000 - 500,000 pbd/annum
Large = >500,000 pbd/annum

Size of hospitals within each hospital type

<table>
<thead>
<tr>
<th>Hospital Type</th>
<th>Percentage (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LTC</td>
<td></td>
</tr>
<tr>
<td>Primary</td>
<td></td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
</tr>
<tr>
<td>Specialist</td>
<td></td>
</tr>
<tr>
<td>Tertiary</td>
<td></td>
</tr>
</tbody>
</table>

Legend:
- Large
- Medium
- Small
- No data
Testing methodology at Participating Hospitals

- **France**: Non toxin detecting method (50%), Toxin alone (30%), Algorithm (not recommended) (20%), Direct toxin detection algorithm (Recommended) (10%)
- **Germany**: No data available
- **Italy**: Non toxin detecting method (60%), Toxin alone (30%), Algorithm (not recommended) (10%)
- **Spain**: Non toxin detecting method (40%), Toxin alone (30%), Algorithm (not recommended) (20%), Direct toxin detection algorithm (Recommended) (10%)
- **UK**: Non toxin detecting method (60%), Toxin alone (30%), Algorithm (not recommended) (10%), Direct toxin detection algorithm (Recommended) (10%)
CDI rates
Reported CDI rates

Kruskall-wallis $p < 0.001$ all groups (except method which is NS)
Kruskall-wallis p <0.001 all groups
Impact of testing density?
Kruskall-wallis $p < 0.001$ for country and type, $p = 0.013$ for size
Is CDI seasonal?
T-test; Italy p = 0.017, Non-toxin = 0.044, Toxin alone = 0.039, all others p>0.05
* $P < 0.05$
Reported CDI rate adjusted for testing rate

* Italy p = 0.02, Toxin alone p = 0.05
Multivariate analysis
Testing rate has the biggest impact on CDI rates, when all other factors are taken into consideration.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Size of effect (95% CI)</th>
<th>Independent variables t value</th>
<th>Significance (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital size</td>
<td>-2.04 (-4.46-0.37)</td>
<td>-1.66</td>
<td>0.098</td>
</tr>
<tr>
<td>Testing method</td>
<td>1.33 (0.31-2.62)</td>
<td>2.01</td>
<td>0.045</td>
</tr>
<tr>
<td>Hospital type</td>
<td>-2.06 (-3.42-0.68)</td>
<td>-2.94</td>
<td>0.003</td>
</tr>
<tr>
<td>Country</td>
<td>0.08 (-0.93-0.95)</td>
<td>0.17</td>
<td>0.986</td>
</tr>
<tr>
<td>Month</td>
<td>-0.18 (-0.48-0.12)</td>
<td>-1.17</td>
<td>0.241</td>
</tr>
<tr>
<td>Number of tests/10,000pbds</td>
<td>0.09 (0.09-0.09)</td>
<td>43.35</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*aDependant variable: CDI cases/10,000pbds*
Summary

• Testing density has the largest effect on reported CDI rates.

• Use of standalone NAAT testing still results in higher CDI rates even when testing density is taken into account
  ▫ This is consistent with a test that may ‘overcall’ true CDI.

• Low testing density can mask the true burden of CDI, such as in long-term healthcare facilities
  ▫ Highlighting the importance of good quality surveillance.

• Lastly, month of testing was not significant in the multivariate model
  ▫ Demonstrating the non-seasonal nature of CDI.
Summary cont...

- Important to understand the context in which published reported rate data have been generated
  - How often hospitals test for CDI
  - How samples are tested for CDI
  - Who is tested for CDI
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  ▫ UK – Prof Mark Wilcox, Georgina Davis, Kerrie Davies
    University of Leeds, Leeds

• Participating Hospitals (n = 200)

• Funder
  ▫ Sanofi Pasteur
Thank you
Any questions?