Denominators for national estimates of antimicrobial use may not work for herds
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Introduction

Problems associated with AMR in humans have led to calls for reduced usage of antimicrobials in agriculture. The setting of targets depends on well-defined “metrics” of usage and they must be appropriate for the group of animals in question.

For a number of herd-years we assess a method for estimating on such metric and the “stability” of this metric – sales of antimicrobial per kg of bovine animal.

Methods

Anonymised veterinary pharmaceutical sales from a Scottish veterinary practice and herd demographic data (via the agricultural census) were collected for 75 cattle herds in the period 2011-2015 leading to 378 complete herd-years of data.

Antimicrobial sales per total kg of bovine were calculated for each herd-year. The denominator was increased by ½ of the minimum value to prevent division by zero (true for 2 observations).

Numerator Results

• Total sales per herd-year were higher in dairy than in beef herds (Table 1)
• Relative variation of antimicrobial sales was higher in beef than in dairy herds

Table 1. Summary statistics for the total weight (g) of active ingredient (a.i.) of antimicrobial sold per herd-year

<table>
<thead>
<tr>
<th>Total weight of antimicrobial (g)</th>
<th>Min</th>
<th>Median</th>
<th>Max</th>
<th>Coefficient of variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef</td>
<td>0.42</td>
<td>362</td>
<td>2215</td>
<td>0.90</td>
</tr>
<tr>
<td>Dairy</td>
<td>4.8</td>
<td>1225</td>
<td>3833</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Denominator Results

• Median weight of bovine per herd-year was higher in dairy than in beef herds (Table 2)
• Relative variation in total weight of animal per herd-year was higher in beef than in dairy herds (Table 2)

Table 2. Summary statistics for the total weight (kg) of animal per herd-year

<table>
<thead>
<tr>
<th>Total weight of animal (kg)</th>
<th>Min</th>
<th>Median</th>
<th>Max</th>
<th>Coefficient of variation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef</td>
<td>0</td>
<td>36915</td>
<td>179445</td>
<td>0.80</td>
</tr>
<tr>
<td>Dairy</td>
<td>2325</td>
<td>73950</td>
<td>179325</td>
<td>0.45</td>
</tr>
</tbody>
</table>

Results of our metric: numerator/denominator

Fig 1. Total weight (kg) of active ingredient (a.i.) of antimicrobial sold and total weight of animal for each herd-year. Colours indicate the percentile range in which the ratio for each point belongs.

• A clear positive relationship between herd size and usage (Fig 1)
• The bottom 5% of sales per kg of animal all had very low total sales (numerator) amongst fairly small herds (Fig 1 – blue dots)
• The top 5% of sales per kg of animal had a wide range of total sales (numerator) amongst fairly small herds (Fig 1 – pink dots)
• The top 1% of sales per kg of animal all came from VERY small herds (Fig 1 – green dots)
• 361 estimates for the sales per kg of animal were in the range 0-50 mg per kg, the remaining 7 observations were in the range 50-350 mg per kg

Table 3. High versus low ratios cross-tabulated with high and low numerator or denominator values. High ratios are predicted by very small denominators (p<10^{-7}) and not by large numerators (p=1)

<table>
<thead>
<tr>
<th>Ratio ≤50 mg/kg</th>
<th>Ratio &gt;50 mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numerator: Weight of a.i. in bottom 90%</td>
<td>324</td>
</tr>
<tr>
<td>Weight of a.i. in top 10%</td>
<td>37</td>
</tr>
<tr>
<td>Denominator: Weight bovine in top 90%</td>
<td>331</td>
</tr>
<tr>
<td>Wt bovine in bottom 10%</td>
<td>30</td>
</tr>
</tbody>
</table>

All 7 with a ratio>50mg/kg had a small denominator

Conclusions

• We chose an inclusive denominator but we still encountered two herd-years with 0kg recorded via the agricultural census
• The importance of unusually low estimates for the denominator is mathematically clear but empirically demonstrated here. Outlying high estimates for usage per kg of animal came from those herd-years with very low total weights of animal.
• Our method seems to work for large herds but is flawed for small herds – this may be because they prescribe in batches
• Standardising usage in relation to herd size is necessary BUT...
• Ratios designed for national-level targets may not be applicable to herd-level targets.

Acknowledgements

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