

Are veterinarians over-using clavulanate in pets?



Analysis of antimicrobial use and beta-lactamase prevalence in animal pathogens

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Background

Amoxiclav is the most commonly used systemic antimicrobial in Australian dogs and cats.

- Some bacteria produce beta-lactamase enzymes, which inactivate amoxicillin; adding clavulanate provides a false substrate for these enzymes, and can preserve the function of amoxicillin.
- Amoxicillin-clavulanate (amoxiclav) is rated as a **medium-importance** antimicrobial in Australia, and **Category C: Caution** in EU.
- A previous study of 4.4 million veterinary consultation records showed that **amoxiclav accounted for one-third of all systemic antimicrobial prescriptions in both dogs and cats** (Figure 1) in Australia
- In contrast, low-importance amoxicillin and trimethoprim-sulfa (TMS) made up just **2%** and **<1%** of prescriptions respectively.

We aimed to establish how frequently the addition of clavulanate to amoxicillin was microbiologically justified.

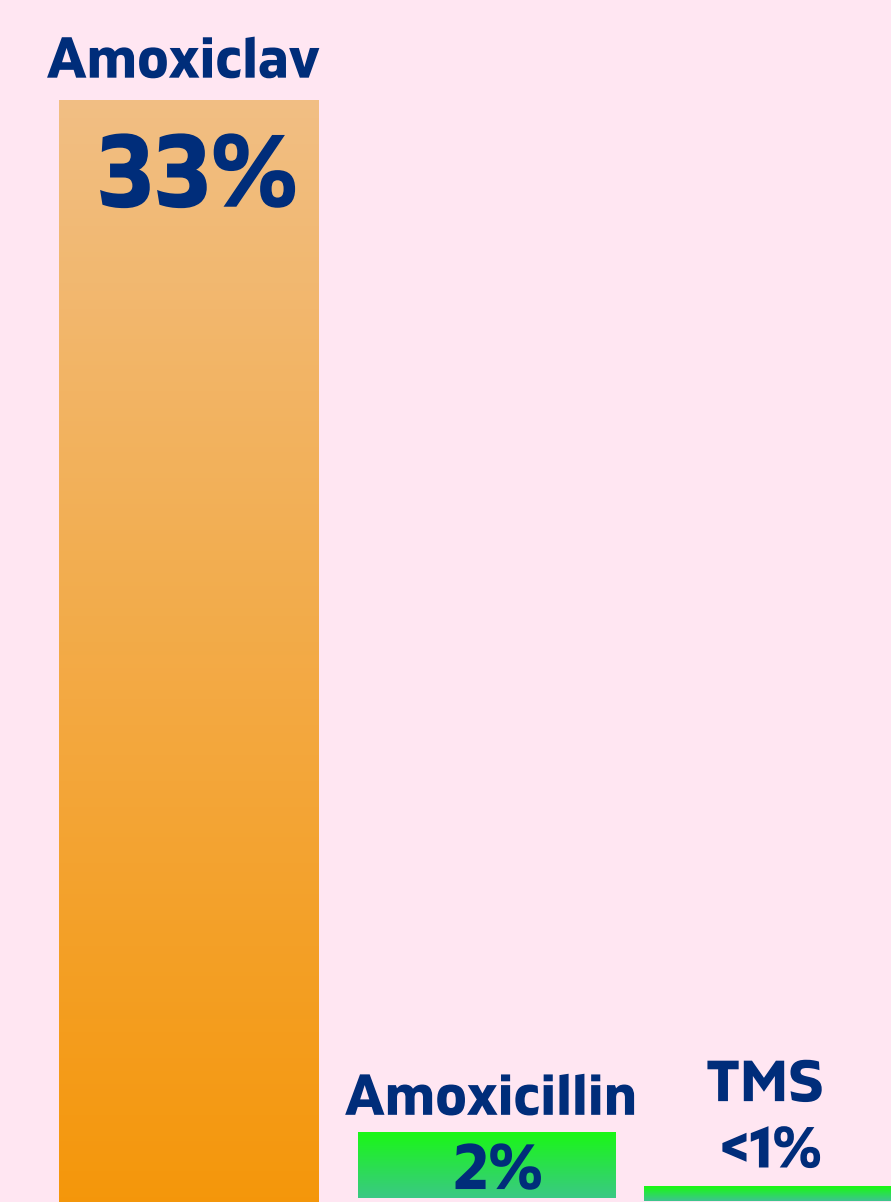


Figure 1: Proportion of cat and dog systemic antimicrobial prescriptions for selected antimicrobials.
 Data from Hur *et al.*, PLoS One 2020
<https://doi.org/10.1371/journal.pone.0230049>

Results

Clavulanate was not often useful; most isolates susceptible to amoxiclav were also susceptible to amoxicillin alone, or to TMS.

Just **6%** of the dog swab isolates and **13%** of cat swab isolates were resistant to **amoxicillin** and susceptible to **amoxiclav** (orange bars)

Only **11%** of the dog urinary isolates and **11%** of cat urinary isolates were resistant to **amoxicillin** and susceptible to **amoxiclav** (orange bars)

Most of the urinary isolates were susceptible to **TMS** (green striped bars) including those resistant to amoxicillin

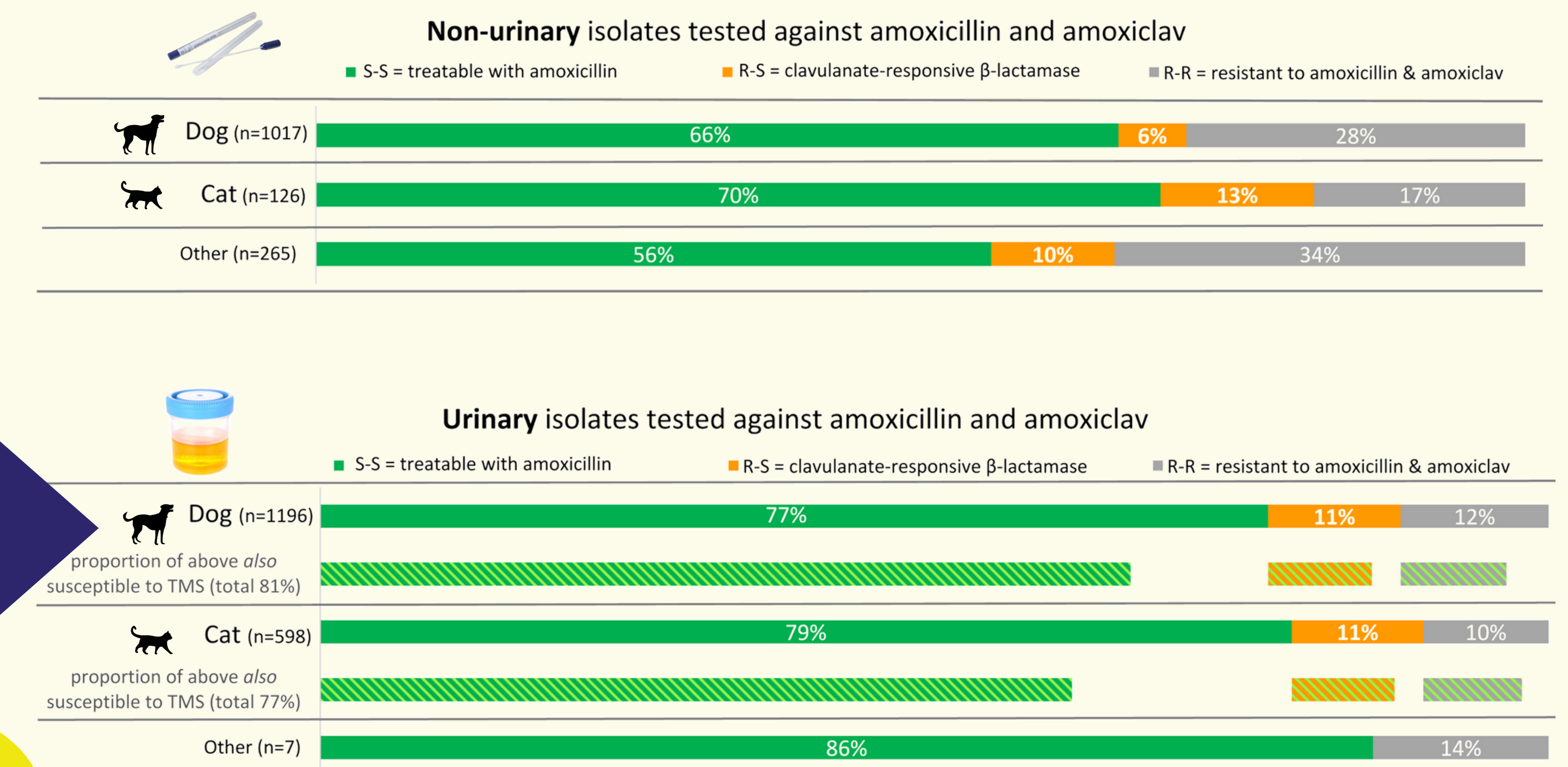


Figure 2: Susceptibility patterns of non-urinary (top) and urinary (bottom) isolates from animals

Methods

We analysed one year of antimicrobial susceptibility results from a veterinary laboratory.

- During this period, the laboratory serviced mostly first-opinion veterinary practices across South-Eastern Australia
- Samples were swabs (body site not specified) and urine samples
- The laboratory used a disc-diffusion method (CDS) to determine antimicrobial susceptibility.

Clavulanate was considered useful when an isolate tested resistant to amoxicillin and susceptible to amoxiclav.



Amoxicillin/Ampicillin: R
 Amoxicillin-clavulanate: S
 = isolate produces clavulanate-responsive beta-lactamase

Discussion

Amoxicillin and TMS are better options.

- Using amoxicillin instead of amoxiclav **reduces dysbiosis** and the risk of other **direct adverse effects**.
- **TMS and amoxicillin are low-importance antimicrobials** in Australia (**Category D: Prudence** in EU) so to minimise **antimicrobial resistance risk**, these are preferred over amoxiclav.
- Hypersalivation from TMS in cats can be prevented by using unbroken, enteric-coated tablets.
- Potential adverse effects of TMS in dogs are largely avoidable by treating for short durations <5 days.

Conclusion

Australian veterinarians could replace most of their amoxiclav use with amoxicillin or TMS.

- The **prevalence of clavulanate-responsive beta-lactamase expression in companion animal isolates was low**.
- **Frequent use of medium-importance amoxicillin-clavulanate** previously identified in Australian companion animal practice is therefore **mostly unnecessary** and likely driven by **habit**
- To preserve antimicrobial effectiveness and reduce adverse effects, veterinarians should change their prescribing behaviour.

