

Figure 1 A proportional representation of intravenous (IV) amoxicillin-clavulanic acid prescriptions documented in the Hospital National Antimicrobial Prescribing Survey (Hospital NAPS) 2013–2021, as compared to IV piperacillin-tazobactam. n = the total number of antimicrobial prescriptions recorded in the Hospital NAPS for that year. Total cumulative prescriptions: IV amoxicillin-clavulanic acid = 2440; IV piperacillin-tazobactam = 14 373.

Prevalence of IV Amoxicillin-Clavulanic Acid Prescriptions

Between 2013 and 2021, IV amoxicillin-clavulanic acid prescriptions notably increased, as indicated in Figure 1, from 0.02% ($n = 2$) of total antimicrobial prescriptions to 2.3% ($n = 698$). This marks a 383.3% increase from 2017 (0.6%), which was the year of the TGA registration of IV amoxicillin-clavulanic acid. In contrast, IV piperacillin-tazobactam decreased between 2013 and 2021 relative to all other antimicrobials, from 6.18% to 5.5%. A notable decrease was also observed from 2016 (6.8%) to 2017 (4.5%).

Guideline Compliance

From the 2440 prescriptions of IV amoxicillin-clavulanic acid between 2013 and 2021, 548 (22.5%) were omitted from the guideline compliance subanalysis as they were non-assessable, guidelines were unavailable, or they were directed therapy. The remaining 1901 prescriptions were included for analysis.

From 2015 to 2021, guideline compliance of IV amoxicillin-clavulanic acid reduced from 85.0% to 66.1% (Figure 2), which is lower than the combined guideline compliance of all other antimicrobial prescriptions excluding IV and oral amoxicillin-clavulanic acid (67.3% in 2021).

Comparatively, Figure 2 demonstrates that oral amoxicillin-clavulanic acid guideline compliance remained relatively steady between those years.

Figure 3 demonstrates guideline compliance in terms of both local and national guidelines between 2015 and 2021. Local guideline compliance reduced from 65.0% to 18.7%, whereas national guideline compliance increased from 20.0% to 47.3%. In 2019, compared to 2018, a notable shift can be appreciated for both local guidelines (53.6% to 22.5%) and national guidelines (15.1% to 39.3%). These findings are complemented by an improvement in overall guideline compliance as demonstrated by Figure 2, increasing from 60.7% to 66.1%.

Appropriateness

From the 2440 prescriptions of IV amoxicillin-clavulanic acid from 2013 until 2021, 40 (1.6%) had appropriateness deemed as 'non-assessable' and were omitted from further analysis. From the 2400 prescriptions available for further analysis, 1893 were deemed appropriate (79.2%), while 486 were deemed inappropriate (20.8%).

In Figure 2, the appropriateness of IV amoxicillin-clavulanic acid is compared with oral amoxicillin-clavulanic acid and the cumulation of all other antimicrobials. From 2016 (96.2%) to 2019 (77.4%),

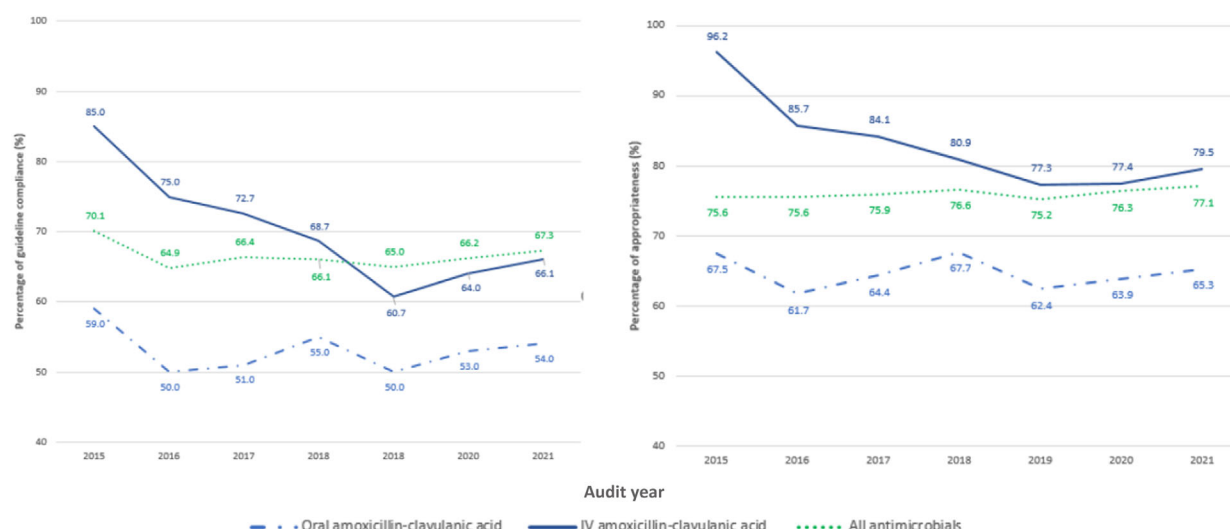


Figure 2 Guideline compliance* and appropriateness^ of amoxicillin-clavulanic acid, comparisons per route and against all other antimicrobials, Hospital NAPS 2015–2021. *n* = the total number of antimicrobial prescriptions recorded in the Hospital NAPS for that year. *Guideline compliance where guidelines were available and assessable (data deemed as ‘directed therapy’, ‘no guidelines available’, or ‘not assessable’ were excluded). Total cumulative prescriptions: IV amoxicillin-clavulanic acid = 1892; oral amoxicillin-clavulanic acid = 9844; all other antimicrobials = 173 558. ^Appropriateness data deemed ‘not assessable’ were excluded. Total cumulative prescriptions: IV amoxicillin-clavulanic acid = 2389; oral amoxicillin-clavulanic acid = 11 852; all other antimicrobials = 206 520.

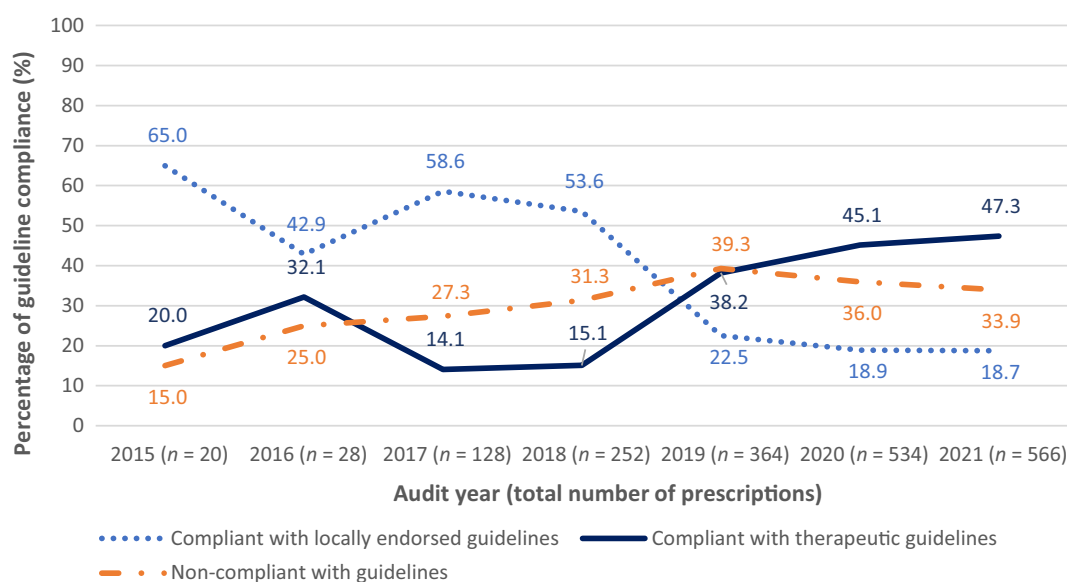


Figure 3 Guideline compliance* of IV amoxicillin-clavulanic acid over time, Hospital NAPS 2015–2021 (*n* = 1892). *n* = the total number of antimicrobial prescriptions recorded in the Hospital NAPS for that year. *Guideline compliance where guidelines were available and assessable (*n* = 548 excluded as ‘directed therapy’, ‘no guidelines available’, or ‘not assessable’).

there was a notable drop in appropriate prescriptions for IV amoxicillin-clavulanic acid. From 2019 to 2021, however, an increase in appropriateness is observed (77.4% to 79.5%). The appropriateness of IV amoxicillin-clavulanic acid consistently remained higher

than the appropriateness of all other antimicrobials over time (2015, 96.2% vs 75.6%; 2021, 79.5% vs 77.1%). The appropriateness of oral amoxicillin-clavulanic acid has similarly also reduced since 2015 from 67.5% to 65.3%. This has been consistently lower than the average.

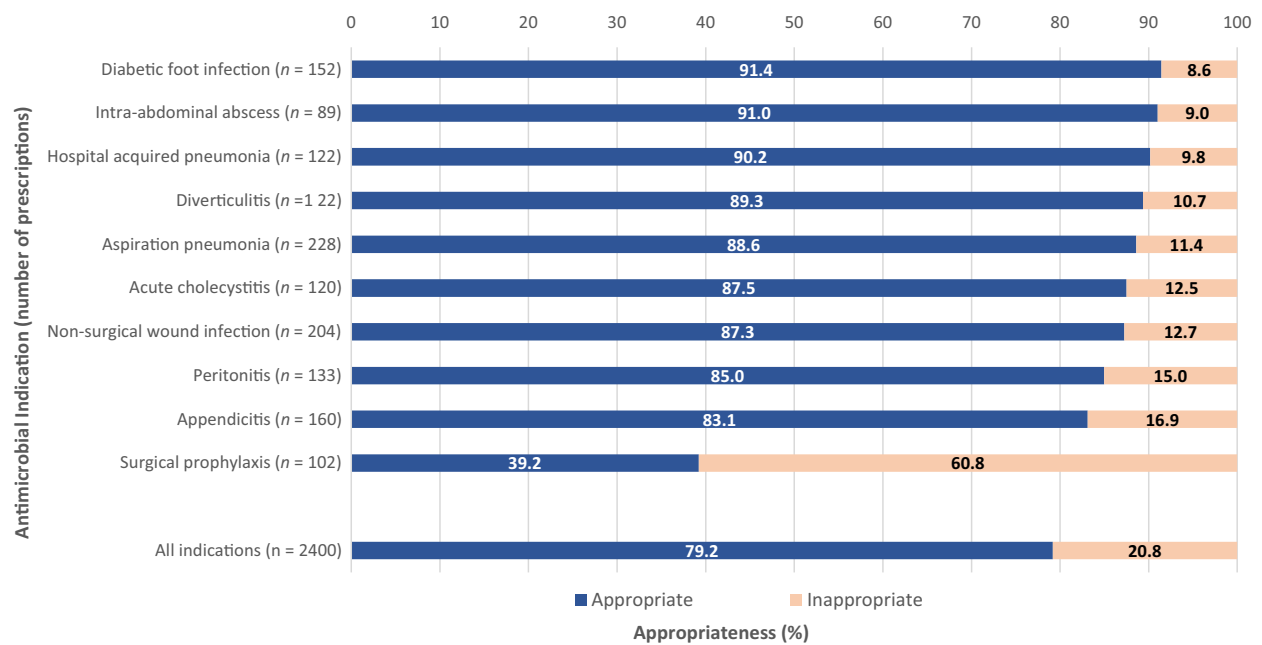


Figure 4 Appropriateness* of IV amoxicillin-clavulanic acid prescriptions ($n = 2400$) per the 10 most common indications, Hospital NAPs 2013–2021. n = the total number of antimicrobial prescriptions per indication. *Appropriateness data deemed ‘not assessable’ were excluded from this analysis ($n = 40$).

Indications

The 10 most common indications for IV amoxicillin-clavulanic acid were selected for further analyses of appropriateness (Figure 4). There were three indications that demonstrated 90.0% or higher rates of appropriateness (diabetic foot infection, intra-abdominal abscess, and hospital-acquired pneumonia). Surgical prophylaxis had a significantly lower rate of appropriateness at 38.8%.

Reasons for Inappropriateness

There were 384 inappropriate prescriptions for IV amoxicillin-clavulanic acid that were deemed to be required. Of these, there were 453 reasons for inappropriateness, as a prescription can have more than one reason for inappropriateness. Unnecessary breadth of spectrum was the most documented reason, accounting for 39.5% of inappropriate IV amoxicillin-clavulanic acid prescriptions. The next most common reason for inappropriate prescribing was incorrect dose or frequency (21.6%).

DISCUSSION

This study demonstrated that over time, IV amoxicillin-clavulanic acid prescriptions are increasing in quantity and declining in quality, thus warranting

initiatives to improve prescribing practices. The increase in use, notably from 2017 onwards, is reflective of the changes in availability and regulation when the TGA first registered IV amoxicillin-clavulanic acid. This change was partly in response to the global shortage of IV piperacillin-tazobactam,¹⁷ evident in Figure 1 as a sharp decline in its use between 2016 (6.8%) and 2017 (4.5%).

The impact of IV amoxicillin-clavulanic acid registration enabled easier access to this antimicrobial, which was previously only accessible through the Australian Special Access Scheme, which ensured use was highly restricted and commonly associated with infectious diseases consultant advice. With the increased access to non-infectious diseases specialist clinicians (on TGA registration in 2017), this policy change has subsequently highlighted the need for, and development of, national guidelines to rationalise its use. Similarly, the costs of these antimicrobials have changed over time and may influence recommendations and restrictions of use at a facility level. For example, one vial of IV piperacillin-tazobactam 4.5 g was worth \$3.30 AUD in comparison to \$20.10 AUD per vial of IV amoxicillin-clavulanic acid 1.2 g. At the end of the study period, in 2021, IV piperacillin-tazobactam cost less than IV amoxicillin-clavulanic acid (\$4.50 AUD vs \$3.20 AUD per vial, respectively). Our study demonstrated a decline in the compliance and appropriateness of IV