

## Antimicrobial allergy ‘labels’ drive inappropriate antimicrobial prescribing: lessons for stewardship

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on behalf of the National Antimicrobial Prescribing Survey (NAPS)

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**Background:** The presence of antimicrobial allergy designations (‘labels’) often substantially reduces prescribing options for affected patients, but the frequency, accuracy and impacts of such labels are unknown.

**Methods:** The National Antimicrobial Prescribing Survey (NAPS) is an annual de-identified point prevalence audit of Australian inpatient antimicrobial prescribing using standardized definitions of guideline compliance, appropriateness and indications. Data were extracted for 2 years (2013–14) and compared for patients with an antimicrobial allergy label (AAL) and with no AAL (NAAL).

**Results:** Among 21 031 patients receiving antimicrobials (33 421 prescriptions), an AAL was recorded in 18%, with inappropriate antimicrobial use significantly higher in the AAL group versus the NAAL group (OR 1.12, 95% CI 1.05–1.22,  $P < 0.002$ ). Patterns of antimicrobial use were significantly influenced by AAL, with lower  $\beta$ -lactam use (AAL versus NAAL; OR 0.47, 95% CI 0.43–0.50,  $P < 0.001$ ) and higher quinolone (OR 2.07, 95% CI 1.83–2.34,  $P < 0.0001$ ), glycopeptide (OR 1.59, 95% CI 1.38–1.83,  $P < 0.0001$ ) and carbapenem (OR 1.74, 95% CI 1.43–2.13,  $P < 0.0001$ ) use. In particular, among immunocompromised patients, AAL was associated with increased rates of inappropriate antimicrobial use (OR 1.68, 95% CI 1.21–2.30,  $P = 0.003$ ), as well as increased use of quinolones (OR 1.88, 95% CI 1.16–3.03,  $P = 0.02$ ) and glycopeptides (OR 1.82, 95% CI 1.17–2.84,  $P = 0.01$ ).

**Conclusions:** AALs are common and appear to be associated with higher rates of inappropriate prescribing and increased use of broad-spectrum antimicrobials. Improved accuracy in defining AALs is likely to be important for effective antimicrobial stewardship (AMS), with efforts to ‘de-label’ inappropriate AAL patients a worthwhile feature of future AMS initiatives.

### Introduction

It is estimated that 10%–30% of patients are designated (or ‘labelled’) as having an allergy to one or more antimicrobials.<sup>1–3</sup> Antimicrobial allergy labels (AALs) represent a heterogeneous group of adverse drug reactions (ADRs), both immune mediated (Type B) and non-immune mediated (Type A) in origin.<sup>4,5</sup> Despite potential variations in pathogenesis, the clinician’s approach to antimicrobial allergy recording and labelling is often the same.<sup>1,2,6,7</sup> While small retrospective studies have suggested that any AAL may be associated with inferior patient outcomes, increased antimicrobial usage, longer antimicrobial duration and increased use of broad-spectrum antimicrobials,<sup>2,3,8,9</sup> this has never been assessed in a large national cohort or considered as a component of antimicrobial stewardship initiatives.

The Australian National Antimicrobial Prescribing Survey (NAPS) collects data on inpatient antimicrobial prescribing from public and private hospitals throughout Australia.<sup>10,11</sup> Using this database, we examined the national prevalence of AALs in Australian inpatients and explored the impact of all AALs on antibiotic usage and the appropriateness of prescribed antibiotics.

### Methods

Data were obtained from the available NAPS database for Australian hospitals from all jurisdictions (August 2013 to December 2014). The NAPS is a standardized electronic auditing tool developed in 2013 to assist health-care facilities monitor antimicrobial prescribing practices and facilitate local quality improvement.<sup>11</sup> Participation is voluntary and data are submitted through a web-based interface to a central database.<sup>12</sup> In 2014,

44% of all public hospital beds were surveyed, from rural to metropolitan centres. Facilities can choose to perform the survey at any time; however, a voluntary annual survey is coordinated in the months surrounding Antibiotic Awareness Week (November annually). Participants may conduct point prevalence surveys of whole hospitals (44%), selected wards or specialities (26%), conduct repeat point prevalence surveys (22%) or randomly selected patients (8%). Ethics approval as a quality assurance project was obtained from the Melbourne Health Human Research Ethics Committee to coordinate the NAPS.

Patient data are included in the NAPS if the patient was prescribed an antimicrobial between 08.00 h and the time of review on the audit day, had received a single dose in the previous 24 h or had received an antimicrobial for surgical prophylaxis in the previous 24 h. Outpatients, day-stay and non-admitted emergency department patients were excluded.<sup>12</sup>

The dataset includes the following: antimicrobial usage (agent, dose, frequency, route, duration); baseline demographics [age, gender, documented antimicrobial allergies, admitting specialty, hospital location, funding type (public/private), bed size]; infection history (infection site, infection type, documentation); compliance with the Australian Antibiotic Guidelines; and antimicrobial appropriateness score.<sup>12,13</sup> As described previously,<sup>12</sup> assessments of antimicrobial appropriateness are undertaken by the staff responsible for antimicrobial stewardship (infectious diseases specialists, clinical microbiologists, other medical practitioners, pharmacists, nurses or infection control practitioners) according to a structured algorithm, and appropriateness is defined as follows: 1 (optimal); 2 (adequate); 3 (suboptimal); 4 (inadequate); or 5 (not assessable).<sup>10,12</sup> The appropriateness algorithm was developed using an expert consensus approach and is based on a composite assessment of: (i) compliance with the national guideline<sup>13</sup> or locally endorsed guidelines; (ii) antimicrobial coverage of causative pathogens; (iii) use of narrow-spectrum antimicrobials where possible; (iv) dosage and/or route; (v) duration if the end date is documented; (vi) allergy mismatch or drug interaction; and (vii) surgical prophylaxis duration <24 h. Patients with poor documentation or who are complex may be classified as non-assessable. A score of 1 or 2 is considered to be 'appropriate' and 3 or 4 as 'inappropriate'. We defined a 'restricted antibiotic' as a third- or fourth-generation cephalosporin, carbapenem, fluoroquinolone or glycopeptide antibiotic. These restricted antibiotics are targets of Australian antimicrobial stewardship programmes. In hospitals without on-site expertise, appropriateness was assessed by the NAPS team. Validation of local and remote assessors has demonstrated that there is agreement between antimicrobial assessment teams.<sup>14</sup>

We divided patients into two groups based upon the presence or absence of an AAL or no AAL (NAAL). All AALs reported were included, and therefore could represent a non-immune (Type A) or immune-mediated (Type B) ADR, according to previous definitions.<sup>5</sup> AAL descriptions were not available for further analysis. Baseline demographics, antimicrobial usage and antimicrobial appropriateness were compared between AAL and NAAL groups. Subgroup analysis was performed for immunocompromised hosts, defined as those admitted under haematology, oncology or stem cell or organ transplantation services.

## Statistical analysis

Categorical variables were summarized and compared between groups using a  $\chi^2$  test. Continuous variables were summarized and compared using Student's *t*-test or the Wilcoxon signed-rank test, as appropriate. A *P* value of <0.05 (two-tailed) was deemed statistically significant. Statistical analyses were performed using Stata 13.0 (StataCorp, College Station, TX, USA).

## Results

### Baseline demographics and AAL prevalence

There were 33 421 antimicrobial prescriptions recorded in 21 031 patients in the NAPS for the study period. When comparing

the AAL and NAAL groups, AAL patients were older 71 (IQR 56–82) versus 65 (IQR 44–78) years,  $P<0.0001$  with a female predominance [2235/3787 (59%) versus 1514/3787 (39%),  $P<0.0001$ ] (Table 1). An AAL was reported in 18% (3787/21 031) of patients, with no difference between public (18%; 505/2778) and private (18%; 3282/18 253) hospital patients, but some difference in AAL prevalence for hospital geographical location (18% major cities, 21% inner regional, 16% outer regional and 8% remote hospitals,  $P<0.0001$ ). Among various inpatient units, the highest AAL prevalence was noted in solid organ transplant (SOT; 25%) and respiratory (25%) units. The AAL prevalences for other identified units were as follows: 24% acute care; 23% infectious diseases; 22% nephrology; 20% general medicine; 19% cancer; 16% orthopaedic surgery; 14% general surgery; 12% obstetrics and gynaecology; 7% trauma and burns; and 3% paediatrics.

### AAL descriptions

The most commonly reported AALs in the AAL group were:  $\beta$ -lactams (13.1%, 2759/21 031), penicillins (8.9%, 1868/21 031), cephalosporins (2.3%, 488/21 031), sulphonamide antibiotics (2.1%, 450/21 031), aminopenicillins (1.4%, 287/21 031), macrolides (1.3%, 271/21 031), tetracyclines (0.8%, 159/21 031), anti-staphylococcal penicillins (0.7%, 152/21 031), fluoroquinolones (0.6%, 125/21 031) and glycopeptides (0.5%, 104/21 031). In patients with a  $\beta$ -lactam allergy, 5.1% (139/2759) reported a concurrent sulphonamide allergy, 1.1% (30/2759) glycopeptide allergy and 2% (57/2759) fluoroquinolone allergy. There was a fluoroquinolone, glycopeptide or sulphonamide allergy label concurrent with  $\beta$ -lactam allergy in 43% (55/127), 28% (30/104) and 31% (139/450) patients, respectively.

### Antibiotic usage

Antibiotic usage for antimicrobial class for AAL and NAAL patients is shown in Figure 1. A higher proportion of AAL patients had more than one recorded non-compliant antimicrobial prescription compared with NAAL patients (21.3% versus 20.8%,  $P=0.0001$ ). The median number of antibiotics prescribed per patient was also higher in AAL than in NAAL patients (1.47 versus 1.44,  $P=0.024$ ). Documentation of antimicrobial indication was similar between AAL and NAAL patients [4461/6174 (72%) versus 19886/27 247 (73%),  $P=0.24$ ], but prescriptions for AAL patients were less concordant with the Australian Antibiotic Guidelines<sup>13</sup> than those of NAAL patients [2713/6309 (43.0%) versus 12 291/27 240 (45.1%),  $P=0.009$ ]. Rates of inappropriate route of antimicrobial administration were similar between AAL and NAAL patients [106/6163 (1.7%) versus 464/27 294 (1.7%),  $P=0.87$ ].

Antibacterial agents constituted 91% of antimicrobial prescriptions, with the proportion of antimicrobials prescribed for AAL and NAAL and shifts towards restricted antibiotic usage demonstrated in Figure 2. The top 10 commonly prescribed antibiotics for both AAL and NAAL groups are shown in Table 2. Ceftriaxone was the most frequently prescribed antibiotic in the AAL group. Not surprisingly,  $\beta$ -lactam antibiotics were prescribed less frequently in the AAL group versus the NAAL group (OR 0.47, 95% CI 0.43–0.50,  $P<0.0001$ ). In the AAL group a higher number of patients were prescribed a fluoroquinolone (OR 2.07, 95% CI 1.83–2.34,  $P<0.0001$ ), glycopeptide (OR

**Table 1.** Baseline demographics for the NAPS cohort

| Cohort demographics              | AAL, N=3787  | NAAL, N=17244 | Total, N=21031 | P      |
|----------------------------------|--------------|---------------|----------------|--------|
| Age (years)                      |              |               |                |        |
| median (IQR)                     | 71 (56–82)   | 65 (44–78)    | 66 (46–79)     | 0.0001 |
| Sex                              |              |               |                |        |
| male                             | 1541 (41)    | 9532 (55)     | 11073 (53)     | 0.0001 |
| Hospital/health service location |              |               |                |        |
| metropolitan                     | 2216 (58.51) | 10150 (58.86) | 12366 (58)     | 0.0001 |
| inner regional                   | 769 (20.3)   | 2821 (16.36)  | 3590 (17)      |        |
| outer regional                   | 238 (6.28)   | 1280 (7.43)   | 1518 (7)       |        |
| remote                           | 66 (1.74)    | 716 (4.15)    | 782 (4)        |        |
| unknown                          | 498 (13.15)  | 2277 (13.20)  | 2775 (13.19)   |        |
| SOT                              |              |               |                |        |
| yes                              | 26 (0.68)    | 77 (0.45)     | 103 (0.49)     | 0.0001 |
| Haematology/oncology             |              |               |                |        |
| yes                              | 234 (6.18)   | 1009 (5.85)   | 1243 (5.9)     | 0.46   |
| Public hospital                  |              |               |                |        |
| yes                              | 3282 (86.67) | 14971 (86.81) | 18253 (86.79)  | 0.82   |
| Antimicrobial indications        |              |               |                |        |
| infection                        |              |               |                |        |
| line related                     | 13 (0.34)    | 36 (0.21)     | 49 (0.23)      |        |
| decolonization                   | 3 (0.08)     | 26 (0.15)     | 29 (0.14)      |        |
| mycobacterial                    | 6 (0.16)     | 31 (0.18)     | 37 (0.18)      |        |
| pyrexia of unknown origin        | 50 (1.32)    | 267 (1.55)    | 317 (1.51)     |        |
| sepsis unspecified               | 210 (5.54)   | 1135 (6.58)   | 1345 (6.39)    |        |
| sexually transmitted             | 40 (1.06)    | 230 (1.33)    | 270 (1.28)     |        |
| travel related                   | 0 (0)        | 10 (0.06)     | 10 (0.05)      |        |
| wound                            | 116 (3.06)   | 593 (3.44)    | 709 (3.37)     |        |
| site                             |              |               |                |        |
| cardiovascular system            | 26 (0.69)    | 136 (0.79)    | 162 (0.77)     |        |
| CNS                              | 24 (0.63)    | 156 (0.90)    | 180 (0.86)     |        |
| ear, nose and throat             | 44 (1.16)    | 236 (1.37)    | 280 (1.33)     |        |
| eye                              | 30 (0.79)    | 142 (0.82)    | 172 (0.82)     |        |
| gastrointestinal system          | 142 (3.75)   | 701 (4.07)    | 843 (4.01)     |        |
| intra-abdominal                  | 150 (3.96)   | 583 (3.38)    | 733 (3.49)     |        |
| oral and dental                  | 89 (2.35)    | 371 (2.15)    | 460 (2.19)     |        |
| respiratory tract                | 940 (24.82)  | 3535 (20.50)  | 4475 (21.28)   |        |
| skin and soft tissue             | 508 (13.41)  | 2041 (11.84)  | 2549 (12.12)   |        |
| urinary tract                    | 463 (12.23)  | 1718 (9.96)   | 2181 (10.37)   |        |
| bone and joint                   | 150 (3.96)   | 679 (3.94)    | 829 (3.94)     |        |
| prophylaxis                      | 606 (16.00)  | 3853 (22.34)  | 4459 (21.20)   |        |
| indication unknown               | 177 (4.67)   | 765 (4.44)    | 942 (4.48)     |        |

Data are *n* (%) unless otherwise indicated.

Note that patients may have had more than one infection or infection site.

1.59, 95% CI 1.38–1.83,  $P < 0.0001$ ), carbapenem (OR 1.74, 95% CI 1.43–2.13,  $P < 0.0001$ ) or cephalosporin (OR 1.13, 95% CI 1.06–1.22,  $P = 0.0004$ ). AAL patients used a high proportion of restricted antibiotics compared with NAAL patients (OR 1.95, 95% CI 1.78–2.15,  $P < 0.0001$ ). Restricted antibiotic usage for patients in respect of reported antibiotic allergies is demonstrated in Figure 3.

### Antibiotic usage in immunocompromised hosts

Among immunocompromised patients, those with an AAL were prescribed more fluoroquinolones (OR 1.92, 95% CI 1.23–3.02,  $P = 0.005$ ), glycopeptides (OR 1.79, 95% CI 1.17–2.73,  $P = 0.01$ ) and carbapenems (OR 2.35, 95% CI 1.50–3.68,  $P = 0.0003$ ) than NAAL patients. In haematology/oncology patients,

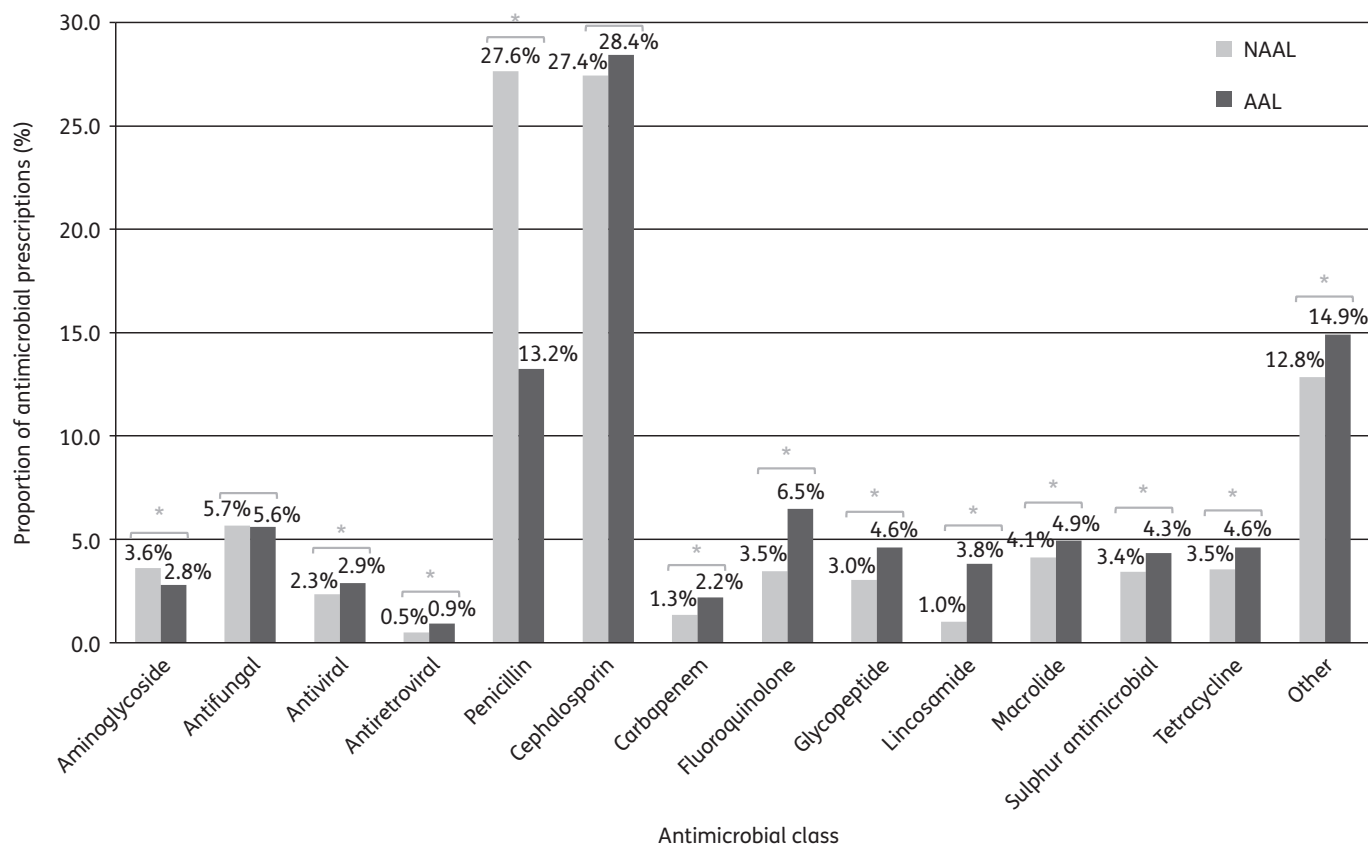


**Figure 1.** Antimicrobial usage for each class for the AAL and NAAL groups. \* $P < 0.05$ .

fluoroquinolone (OR 1.88, 95% CI 1.16–3.03,  $P = 0.02$ ), glycopeptide (OR 1.82, 95% CI 1.17–2.84,  $P = 0.01$ ), carbapenem (OR 2.15, 95% CI 1.34–3.46,  $P = 0.002$ ) and cephalosporin (OR 1.64, 95% CI 1.15–2.36,  $P = 0.009$ ) antibiotics made up a higher proportion of antimicrobial prescriptions in AAL patients compared with NAAL patients. In SOT patients, there was no statistically significant difference in fluoroquinolone (OR 0.55, 95% CI 0.17–0.18,  $P = 0.33$ ), glycopeptide (OR 0.82, 95% CI 0.23–2.82,  $P = 0.75$ ) or cephalosporin (OR 0.93, 95% CI 0.3–2.9,  $P = 0.91$ ) usage, but a significant increase in carbapenem use was noted in the AAL group (OR 2.15, 95% CI 1.39–3.45,  $P = 0.03$ ).

**Antimicrobial appropriateness**

The rates of inappropriate antimicrobial prescribing for AAL and NAAL patients are shown in Table 3. Overall, a higher rate of inappropriate prescribing was observed among AAL versus NAAL patients (OR 1.12, 95% CI 1.05–1.22,  $P < 0.002$ ). Furthermore, rates for AAL patients remained higher even if prescriptions for prophylactic antimicrobials were excluded (OR 1.14, 95% CI 1.05–1.24,  $P = 0.002$ ) and among immunocompromised patients [OR 1.68, 95% CI 1.21–2.30,  $P = 0.003$ ; haematological malignancy and/or cancer (OR 1.47, 95% CI 1.046–2.075,  $P = 0.032$ ) and SOT (OR 2.72, 95% CI 1.06–6.98,  $P = 0.046$ )]. Inappropriate prescribing was also more common among AAL patients within

private compared with public hospitals (OR 1.17, 95% CI 1.074–1.26,  $P = 0.0003$ ).

**Discussion**

Based on this large national survey, approximately 1 in 5 patients (18%) have an AAL—a considerable clinical burden considering the inferior outcomes associated with such a designation.<sup>1,3,8,9</sup> In particular, we noted that patients designated with an AAL were associated with high rates of inappropriate antimicrobial use. This is especially concerning for immunocompromised patients, given the potentially serious implications of any infections and the enhanced risk of colonization with multi-resistant pathogens.<sup>8</sup> Previous authors have highlighted the fact that many reported antibiotic ‘allergies’ are in fact drug intolerance (Type A), or distant unknown reactions unlikely to be replicated on skin-prick testing or oral challenge.<sup>2,15</sup> Among patients with reported antimicrobial allergy (primarily to  $\beta$ -lactams), only 10%–20% are positive on formal testing.<sup>16,17</sup> Given this and the potential consequences of an incorrect AAL, accurate assessment for true antibiotic allergy could now be considered a potentially important antibiotic stewardship issue, with the aim of undertaking antimicrobial allergy de-labelling where appropriate.

AAL prevalence varied greatly between admitting units, being highest in SOT and respiratory patients (25%) and (perhaps not surprisingly) lowest in paediatric patients (3%). In a retrospective

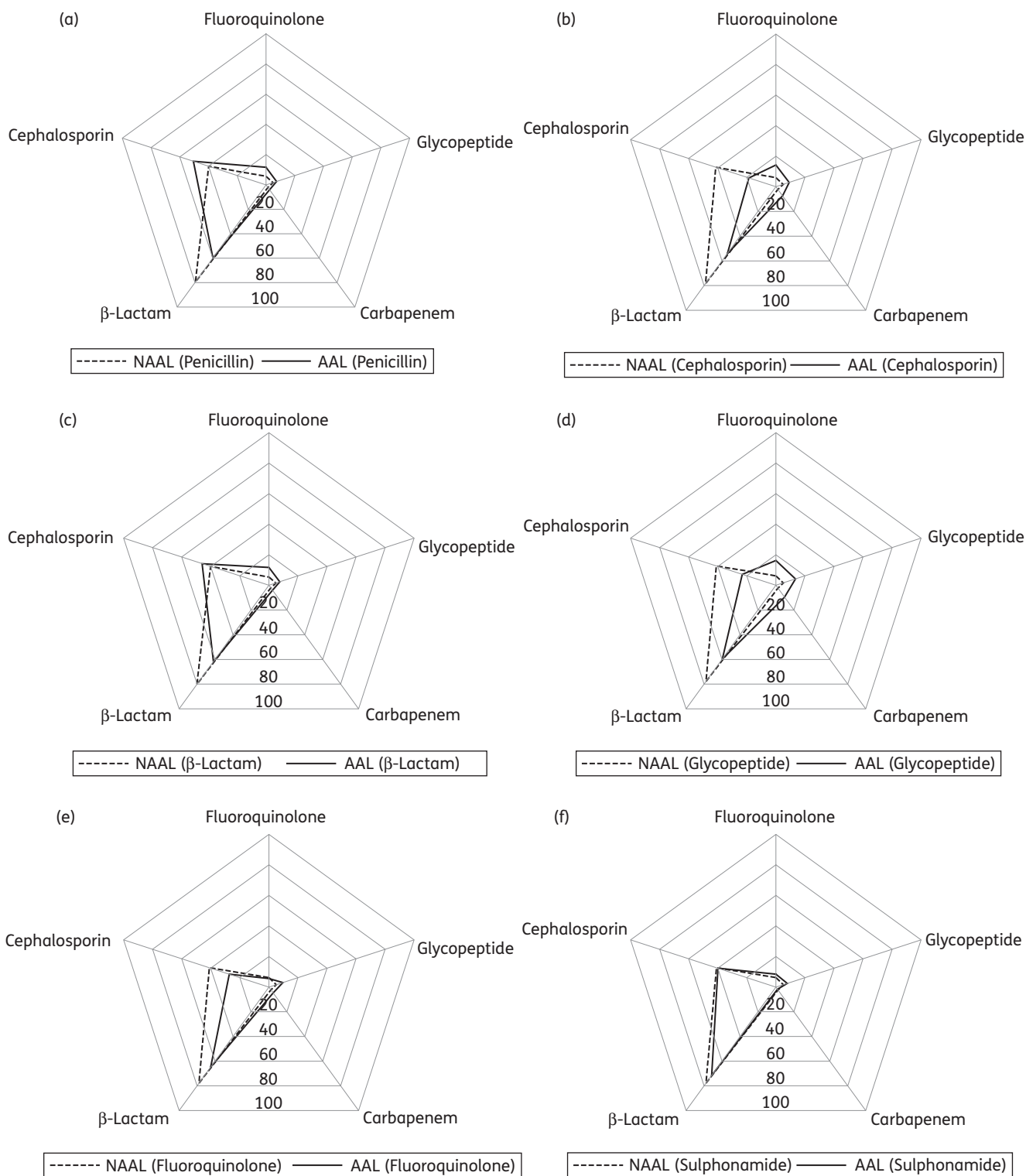


**Figure 2.** Antimicrobial usage (proportion of total prescriptions) in reference to a particular AAL demonstrated via radar plots. (a) Penicillin allergy. (b) Cephalosporin allergy. (c)  $\beta$ -Lactam allergy. (d) Glycopeptide allergy. (e) Fluoroquinolone allergy. (f) Sulphonamide allergy.

cohort of general surgical and medical patients AAL prevalence was estimated to be 11%, while in a group of cancer patients it was 23%.<sup>3,9</sup> The units with the highest prevalence are potentially key targets for antimicrobial allergy de-labelling programmes. The rate of antimicrobial allergy captured via NAPS reflects the real-world reporting of allergy labels, since it includes both Type

**Table 2.** Top 10 antibiotics prescribed in the AAL and NAAL groups

| Number | AAL group, number of prescriptions for each agent (%);<br>total number of antimicrobial prescriptions=6174 |            | NAAL group, number prescriptions for each agent (%); total<br>number of antimicrobial prescriptions=27247 |             |
|--------|------------------------------------------------------------------------------------------------------------|------------|-----------------------------------------------------------------------------------------------------------|-------------|
| 1      | ceftriaxone                                                                                                | 706 (11.4) | cefazolin                                                                                                 | 3140 (11.5) |
| 2      | cefazolin                                                                                                  | 481 (7.8)  | ceftriaxone                                                                                               | 2614 (9.6)  |
| 3      | metronidazole                                                                                              | 428 (6.9)  | metronidazole                                                                                             | 1836 (6.7)  |
| 4      | cefalexin                                                                                                  | 373 (6.1)  | piperacillin/tazobactam                                                                                   | 1797 (6.6)  |
| 5      | doxycycline                                                                                                | 283 (4.6)  | amoxicillin/clavulanate                                                                                   | 1722 (6.3)  |
| 6      | vancomycin                                                                                                 | 275 (4.5)  | flucloxacillin                                                                                            | 1383 (5.1)  |
| 7      | ciprofloxacin                                                                                              | 245 (3.9)  | cefalexin                                                                                                 | 1255 (4.6)  |
| 8      | piperacillin/tazobactam                                                                                    | 230 (3.7)  | doxycycline                                                                                               | 960 (3.5)   |
| 9      | azithromycin                                                                                               | 229 (3.7)  | benzylpenicillin                                                                                          | 909 (3.3)   |
| 10     | amoxicillin/clavulanate                                                                                    | 190 (3.1)  | gentamicin                                                                                                | 895 (3.3)   |

**Table 3.** Appropriateness in relation to patient AAL (N=20093)

| Patient AAL                          | Inappropriate prescribing, n (%) | OR (95% CI)       | P     |
|--------------------------------------|----------------------------------|-------------------|-------|
| <b>β-Lactam</b>                      |                                  |                   |       |
| yes                                  | 883/2639 (33.45)                 | 1.143 (1.05–1.25) | 0.003 |
| no                                   | 5334/17454 (30.56)               |                   |       |
| <b>Penicillin</b>                    |                                  |                   |       |
| yes                                  | 617/1789 (34.48)                 | 1.194 (1.08–1.32) | 0.001 |
| no                                   | 5600/18304 (30.60)               |                   |       |
| <b>Aminopenicillin</b>               |                                  |                   |       |
| yes                                  | 90/287 (31.35)                   | 1.013 (0.79–1.30) | 0.97  |
| no                                   | 6127/19851 (30.86)               |                   |       |
| <b>Antistaphylococcal penicillin</b> |                                  |                   |       |
| yes                                  | 40/142 (28.17)                   | 0.88 (0.61–1.26)  | 0.53  |
| no                                   | 6177/19951 (30.96)               |                   |       |
| <b>Cephalosporin</b>                 |                                  |                   |       |
| yes                                  | 123/414 (29.71)                  | 1.06 (0.86–1.31)  | 0.63  |
| no                                   | 4517/15844 (28.51)               |                   |       |
| <b>Glycopeptide</b>                  |                                  |                   |       |
| yes                                  | 15/91 (16.48)                    | 0.49 (0.28–0.86)  | 0.02  |
| no                                   | 4625/16167 (28.61)               |                   |       |
| <b>Fluoroquinolone</b>               |                                  |                   |       |
| yes                                  | 31/113 (27.43)                   | 0.94 (0.63–1.43)  | 0.88  |
| no                                   | 4609/16145 (28.55)               |                   |       |
| <b>Sulphonamide</b>                  |                                  |                   |       |
| yes                                  | 146/429 (34.03)                  | 1.16 (0.94–1.41)  | 0.17  |
| no                                   | 6071/19664 (30.87)               |                   |       |

B ADRs (immune mediated, on target effects) and Type A ADRs (non-immune-mediated, off-target effects).<sup>18</sup> Moskowitz et al.<sup>7</sup> demonstrated that 36% of electronic allergy records lacked an allergy description, preventing prescribers from being able to discern between true allergies and drug side effects. We have previously

estimated from a single-centre NAPS experience that almost 25% of antibiotic ‘allergies’ are likely Type A and another 25% unknown.<sup>15</sup> Therefore, we postulate that a large portion of our antibiotic allergy labels would be unsubstantiated in medical records and of non-immune origin, leaving scope for greater allergy documentation and de-labelling to improve the quality of prescribing.

Utilizing the NAPS structured appropriateness scale we demonstrated that inappropriate prescribing was higher in patients with an AAL. More pronounced was the difference in appropriateness amongst the highest users of antimicrobials—patients with haematological malignancy or cancer. Potentially, the removal of antimicrobial labels in these groups may aid appropriateness measures. It was not surprising that in patients with a β-lactam AAL there was a significant reduction in the utilization of all β-lactams. When further examining the AAL group there was a notably higher proportion of fluoroquinolones, glycopeptides, cephalosporins and lincosamides used.

This study has some limitations. Firstly, by examining only inpatient AALs we were unable to accurately differentiate between Type A and B ADRs. While a standardized protocol (an internally validated tool for assessing antibiotic appropriateness) is provided to participating NAPS hospitals, variation in clinician interpretation is expected. While most hospitals performed hospital-wide surveys, targeted units may have been surveyed at some centres. We defined a restricted antibiotic based upon Australian antimicrobial stewardship targets, which may differ from those used in other centres. Furthermore, an assessment of restricted antibiotic use in immunocompromised hosts is confounded by the empirical use of broad-spectrum antibiotics as first-line therapy for febrile neutropenia (e.g. cefepime, piperacillin/tazobactam). There is the potential for ascertainment bias, as the more antimicrobials patients receive, the greater may be the likelihood of obtaining an AAL. Nonetheless, this multi-site prospective NAPS study does provide a valuable estimate of the national AAL burden and its impact on antimicrobial prescribing patterns.

Given our findings, we believe antibiotic allergy clinics and de-labelling programmes, which have been shown to be highly successful in accurately and safely removing allergy labels, should be considered as an important component of national

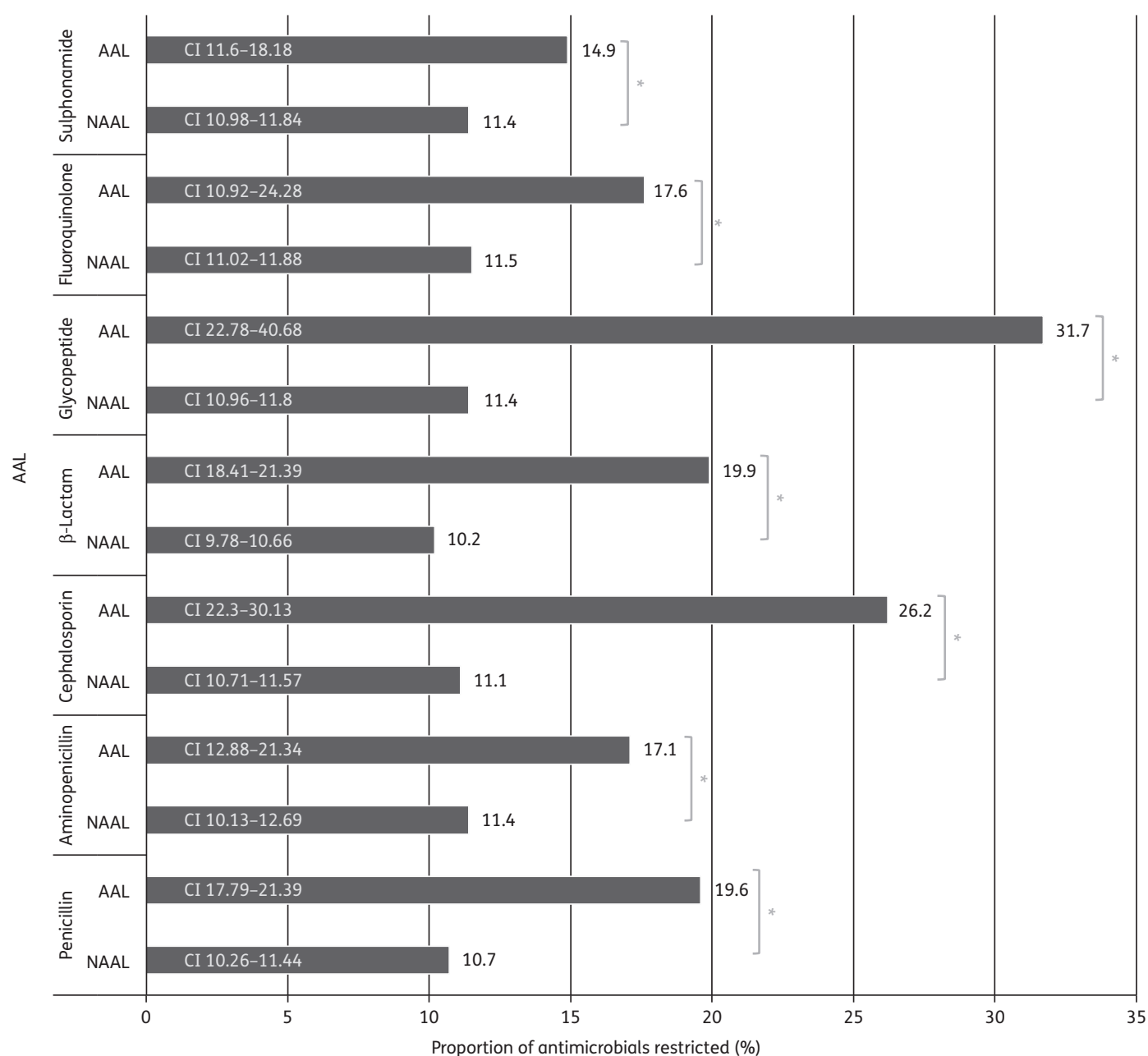


**Figure 3.** Proportion of antibiotics employed that are restricted, in patients with various AALs. \* $P < 0.01$ . CI, 95% CI.

stewardship initiatives.<sup>16</sup> Models have been proposed of the integration of antibiotic allergy services into stewardship programmes to improve antibiotic utilization.<sup>2,19,20</sup> A small number of pilot studies have demonstrated an increase in  $\beta$ -lactam uptake and reduced antimicrobial costs with inpatient penicillin skin-prick testing,<sup>21,22</sup> while pharmacy referral to skin-prick testing and physician education programmes have also improved  $\beta$ -lactam usage.<sup>23,24</sup> A solution to AALs may lie in coordinated approaches, incorporating inpatient and outpatient allergy testing and improving electronic allergy recording, antimicrobial stewardship allergy identification and both infectious disease and allergy physician

engagement.<sup>7,25</sup> Antibiotic allergy should remain a priority issue for infectious diseases physicians, who are often required to consult and manage patients with complex antimicrobial allergy histories.

### Conclusions

In an era of increasing antimicrobial resistance and a diminishing antibiotic pipeline the appropriate use of antibiotics has never been more important. We demonstrate that AALs remain highly prevalent in Australian inpatients and are associated with

inappropriate and excess antimicrobial prescribing. This supports the consideration of targeted antimicrobial stewardship initiatives involving antibiotic allergy de-labelling programmes.

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## Transparency declarations

None to declare.

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