RESEARCH ARTICLE

Impact of expired stock on antimicrobial surveillance in rural hospitals: implications and challenges for stewardship

Georgia Macauley1,*, Michelle Penny2, Vicki McNeil3, Tanja Gustafsson3, Nadine Hillock3

1 School of Pharmacy and Medical Sciences, University of South Australia, Adelaide, Australia
2 Riverland General Hospital, Berri, Australia
3 Communicable Disease Control Branch, Department for Health and Wellbeing, Adelaide, Australia

Abstract

Background: Quantitative surveillance of antimicrobial use is a valuable tool used to support antimicrobial stewardship, identify overprescribing, monitor unexpected changes in usage, and assess the impact of interventions to improve prescribing. Smaller, more remote hospitals face many challenges in conducting effective antimicrobial surveillance.

Aim: To investigate the impact of expired stock on reported antimicrobial usage rates in smaller, more remote hospitals.

Method: Antimicrobial usage rates (defined daily doses [DDDs] per 1000 occupied bed days [OBDs]) were calculated using monthly dispensing data and hospital activity data from 12 rural South Australian facilities for the period January 2018 to December 2020. Usage rates were re-calculated, excluding expired stock, to estimate the impact expired stock had on reported usage rates and to quantify stock wastage.

Results: Between 2018 and 2020, the average monthly aggregate usage rate for all 12 hospitals was 650 DDD/1000 OBDs, with the exclusion of expired stock resulting in an average monthly reduction of 37 DDD/1000 OBDs (5.7%). Analysis by the Australian Institute of Health and Welfare peer group demonstrated that the exclusion of expired stock reduced average monthly usage rates by 6.0% for Public Acute Group C sites and 10.6% for Public Acute Group D and Very Small Hospitals.

Conclusion: Replacement of expired stock may account for a substantial proportion of perceived antimicrobial usage in rural and remote hospitals, particularly for agents infrequently prescribed. Pharmacy distribution data is a surrogate measure for actual patient consumption; utilisation reports for smaller rural facilities should be interpreted with acknowledgment of the challenges of stock management in remote locations.

Keywords: antimicrobial stewardship, rural, hospital, antimicrobial surveillance, antibiotic surveillance.

INTRODUCTION

Antimicrobial surveillance is an important tool for stewardship, enabling the monitoring of trends in antimicrobial usage and unexpected changes in prescribing practices.1 Quantitative measurement of antimicrobial use requires a standardised metric to reflect the volume of use and allow benchmarking between similar hospitals or settings.2 In Australia, hospital usage is monitored by the National Antimicrobial Utilisation Surveillance Program (NAUSP) using volume-based surveillance, allowing hospitals to benchmark their usage rates with similar acuity hospitals across Australia.3 Contributor hospitals upload monthly antimicrobial usage obtained from pharmacy dispensing and distribution data, as well as hospital activity data, to the NAUSP portal. This data is used to generate antimicrobial usage rates, which hospitals can use to identify overuse or unusual use of antimicrobial agents.

Hospitals in Australia are classified by the Australian Institute of Health and Welfare (AIHW) based on their size and acuity for the purpose of comparing hospital statistics and performance.4 Hospitals are assigned to peer groups with others that share similar characteristics to provide a basis for more meaningful comparisons. NAUSP uses AIHW peer groups for the purpose of benchmarking, which allows hospitals to compare antimicrobial usage rates with other similar hospitals across Australia, or within their state or territory.

The Priority Antibacterial List (PAL) was compiled and published in 2020 as an additional tool designed to support antimicrobial stewardship by identifying
antimicrobial agents of critical importance in human health.\textsuperscript{5} Antibacterial agents are categorised via an Access, Curb, and Contain classification system, based on their preferred place in therapy and their potential for antimicrobial resistance (AMR). Antibacterial agents included in the Access category are generally recommended as first-line treatment for common infections and have a low AMR or healthcare-associated infection (HAI) potential. The Curb category generally includes first-line treatments for common infections with a high AMR potential. Agents classified in the Contain category have a high AMR or HAI potential and are not recommended as first-line therapy for common bacterial infections.\textsuperscript{5}

In smaller, regional, and remote health facilities, antimicrobial stewardship can be challenging due to a number of factors, including limited or absent pharmacy resources, lack of access to on-site infectious diseases (ID) expertise, and geographical location from larger centres.\textsuperscript{6} In regional areas with lower population density, demand for hospital services can often fluctuate quite substantially.\textsuperscript{7} Fluctuation in patient activity data can make it difficult to identify trends and unexpected changes in antimicrobial surveillance data over time. Moreover, the usage of restricted agents, as reported by NAUSP, can be proportionately higher in smaller hospitals for reasons that are often unclear.\textsuperscript{8} In addition to challenges associated with variable patient activity in more remote hospitals, stock management and ensuring timely access to appropriate antimicrobials is also problematic. If appropriate antimicrobials are unavailable when they are required, this can lead to inappropriate use of alternative agents, therefore smaller hospitals must ensure these antimicrobials are stocked even if they are rarely used.

Whilst many barriers to antimicrobial stewardship in smaller, more remote hospitals have been recognised,\textsuperscript{9–12} an area currently not well explored is the proportion of antimicrobial usage that can be attributed to replacing expired stock. Studies demonstrate that anti-infectives, particularly systemic anti-bacterial agents and anti-viral agents, are among the most common agents to expire from hospital shelves.\textsuperscript{13} Due to the nature of national hospital surveillance methods, with usage rates being generated from hospital dispensing reports, the replacement of expired stock may contribute to a considerable proportion of antimicrobial ‘usage’.

NAUSP reports show that from mid-2017, Public Acute Group C hospital usage of reserve-line, narrow-spectrum antibacterial agents was more than double the usage rates of Public Acute Group B hospitals, and almost as high as usage rates for Public Acute Group A hospitals.\textsuperscript{14} By late 2018, Public Acute Group C hospitals’ usage of reserve-line, narrow-spectrum agents exceeded that of Public Acute Group A. Reserve-line agents are typically less frequently prescribed, especially among smaller hospitals, but as previously discussed, maintaining adequate levels of stock is important.

The Riverland Mallee Coorong Local Health Network (RMCLHN), located in South Australia (SA), is a rural network consisting of 12 hospital facilities. The network consists of five Public Acute Group C hospitals, five Public Acute Group D hospitals, and two Very Small Hospitals, as classified by the AIHW. The RMCLHN is unique in SA in that all expired stock across these facilities is periodically recorded electronically. This provides the opportunity to estimate the impact of expired stock on antimicrobial surveillance rates in these smaller hospitals.

The purpose of this study was to quantify the proportion of antimicrobial usage in the RMCLHN that can be attributed to the replacement of expired stock over the three-year period from January 2018 to December 2020. The primary objective was to measure antimicrobial usage surveillance rates with and without consideration of expired stock to estimate the overall impact of expiries on utilisation rates. A secondary objective was to estimate the costs associated with expired, unused antimicrobials in these rural and remote hospitals over the three-year period.

METHOD

Usage rates generated by NAUSP are reported as defined daily doses (DDDs) per 1000 occupied bed days (OBDs). The DDD is a unit of measure assigned to drugs by the World Health Organization (WHO) for standardisation purposes to allow for comparisons between agents at the local, national and international level. The DDD is defined as the “assumed average maintenance dose per day for its main indication in adults.”\textsuperscript{15} OBDs refer to the total sum of bed days of all admitted patients accommodated during the reporting period, reported from the total number of inpatients at midnight each day.

Antimicrobial usage rates (DDDs per 1000 OBDs) were calculated using monthly dispensing data from the 12 healthcare facilities across the RMCLHN for January 2018 to December 2020. Usage rates were then recalculated excluding expired stock to estimate the impact of expired stock on reported usage rates and to quantify the amount of wastage generated between 2018 and 2020. Antimicrobials were grouped into their PAL...
category for analysis of usage rates and the proportional rates of expired stock by PAL category.

The average and median monthly OBDs for each of the hospitals was calculated for the three-year period to illustrate the usual hospital activity at each of the sites.

Finally, the annual cost of expired antimicrobials over the three-year period was calculated using the average weighted cost and stratified by AIHW peer group.

RESULTS

Patient Activity Data

Table 1 summarises the average, median monthly OBDs, and interquartile ranges for each RMCLHN hospital from January 2018 to December 2020. In 2018 and 2019, total OBDs across all hospitals combined were 41,584 and 41,600, respectively. In 2020, OBDs reduced to 36,971.

Amount of Antimicrobial Wastage due to Expiry

Overall, the expired antimicrobial stock generated between January 2018 and December 2020 consisted of 50 antimicrobial agents, comprising 111 different antimicrobial products.

The total quantity of antimicrobials (represented as total DDDs) dispensed over the three-year period is illustrated in Figure 1. Table 2 provides the number of DDDs dispensed and the amount that expired each year for each antimicrobial class. Overall, the antimicrobial classes that contributed the largest total number of DDDs wasted across the three-year period were penicillins, macrolides, fluoroquinolones, and lincosamides. The classes with the highest proportion of DDDs wasted were lincosamides (25.2%), fluoroquinolones (16.8%), and antifungals (13.6%).

Effect of Expired Stock on Usage Rates

When considering expired stock, on average over the three years, the average monthly antimicrobial usage rate reduced from 650 DDDs/1000 OBDs to 613 DDDs/1000 OBDs, an average reduction of 5.6% across all 12 hospitals. The percentage of expired stock each month was greater in 2020 (9.4% on average) compared to 4% over 2018 and 2019 combined.

Figure 2 shows the aggregate usage rates according to AIHW peer group, calculated by including all dispensed antimicrobials, as well as usage rates accounting for expired stock. The average monthly usage rate across RMCLHN Public Acute Group C hospitals (n = 5) was 625 DDDs/1000 OBDs, which reduced to 588 DDDs/1000 OBDs when accounting for expired stock. In Public Acute Group D (n = 5) and Very Small Hospitals (n = 2), the combined average monthly usage rate reduced from 734 DDDs/1000 OBDs to 662 DDDs/1000 OBDs when expired stock was considered. Thus, on average the monthly reduction in usage rates with consideration of expired stock was 6.0% in Public Acute Group C facilities and 10.6% for Public Acute Group D and Very Small Hospitals.

When analysing the impact of expired stock by PAL category, consideration of expired stock resulted in the total monthly usage rates across all 12 hospitals for Access category agents reduced on average from 315 DDDs/1000 OBDs to 296 DDDs/1000 OBDs (6.1% reduction). The total monthly usage rate of Curb agents reduced on average from 334 DDDs/1000 OBDs to 318 DDDs/1000 OBDs (4.7% reduction). Monthly usage of Contain agents reduced on average from 2.6 DDDs/1000 OBDs to 1.9 DDDs/1000 OBDs, a relative reduction of 26%.

Costs Associated with Expired Antimicrobials

The average annual cost of expired stock was $8,790 over the three-year period. Analysis by the AIHW peer group showed the average annual cost of expired stock generated for Public Acute Group C over the three-year period was $5,697. The average annual cost of expired stock for Public Acute Group D and Very Small Hospitals was $3,092 over the three-year period.
Total Defined Daily Doses dispensed/distributed by antimicrobial class, 2018-2020

Proportion of total DDDs dispensed/distributed that expired by drug class

Figure 1 Defined daily doses distributed or dispensed in RMCLHN 2018–2020 (% expired shown above each column). DDD = defined daily dose.

Table 2 Amount dispensed (DDDs) per year and amount expired, by antimicrobial class

| Antimicrobial Class                  | 2018  | 2019  | 2020  |
|--------------------------------------|-------|-------|-------|
|                                      | DDDs dispensed | DDDs expired (%) | DDDs dispensed | DDDs expired (%) | DDDs dispensed | DDDs expired (%) |
| Carbapenems                          | 21.0  | 3 (14.3%) | 49.7  | 11 (22.1%) | 40.0  | 0 (0.0%) |
| Antifungals                          | 120.5 | 2 (1.7%)  | 251.8 | 30 (11.9%) | 274.0 | 56 (20.4%) |
| Glycopeptides                        | 146.5 | 10 (7%)   | 335.5 | 6 (1.9%)  | 204.0 | 56 (20.4%) |
| Sulfonamide-Trimethoprim Combination | 192.0 | 1 (0.7%)  | 311.0 | 10 (3.1%) | 348.3 | 10 (2.7%) |
| Lincosamides                         | 178.6 | 32 (17.9%)| 410.1 | 68 (16.5%)| 440.0 | 160 (36.2%)|
| Fluoroquinolones                     | 410.8 | 43 (10.5%)| 720.8 | 140 (19.4%)| 651.8 | 117 (18%)  |
| Trimethoprim                         | 867.0 | 8 (1.0%)  | 951.8 | 6 (0.6%)  | 734.3 | 3 (0.4%)  |
| Aminoglycosides                      | 941.8 | 13 (1.4%) | 1062.1| 54 (5.1%) | 813.5 | 93 (11.5%) |
| Macrolides                           | 2335.8| 310 (13.3%)| 2300.4| 197 (8.5%)| 1955.3| 143 (7.3%) |
| Third- and fourth-generation cephalosporins | 2087.5| 26 (1.2%) | 2441.6| 18 (0.7%) | 2145.5| 43 (2%)   |
| Tetracyclines                        | 2574.5| 11 (0.4%) | 3424.5| 2 (0.0%)  | 1910.0| 25 (1.3%) |
| First- and second-generation cephalosporins | 4303.0| 76 (1.8%) | 4631.4| 123 (2.7%)| 4696.7| 176 (3.9%) |
| Penicillins                          | 6765.5| 392 (5.8%)| 6936.7| 374 (5.4%)| 6650.6| 579 (8.7%)|

DDD = defined daily dose.
DISCUSSION

This is the first study to investigate the impact of expired stock on reported antimicrobial usage rates in regional, rural, and remote hospitals. These results help provide further insight into the challenges of maintaining appropriate stock levels in rural and remote locations, and provide an estimate of stock lost to expiry for consideration when interpreting benchmarking reports. Many smaller, remote hospitals have no on-site pharmacy service and the service models in rural areas of Australia are diverse, with varying levels of resourcing.\textsuperscript{11} Despite not having onsite pharmacy services, smaller remote sites are still required to meet safety and quality standards for medicines management to ensure safe patient care.\textsuperscript{15} Some rural and remote hospitals have such low levels of patient occupancy that it is difficult to show significant changes in antimicrobial usage rates over time. Stock management in rural locations is a balance of ensuring recommended antimicrobials are available when required, while ensuring avoidance of unnecessary over-stocking. For some infections, the time to antimicrobial administration has a significant impact on outcomes, with delays in treatment increasing the risk of mortality.\textsuperscript{16} If appropriate antimicrobials are not available when required, there is a risk that inappropriate alternatives will be used. However, in some rural locations the risk of stock being unused has resulted in some antimicrobials not being kept on hand.\textsuperscript{10} In addition, the findings in this study demonstrate that accounting for expired stock can result in visible reductions of reported antimicrobial usage rates generated from smaller hospitals.

Current NAUSP methodology for calculating usage rates uses hospital dispensing and distribution reports as a surrogate for antimicrobial consumption. A limitation of this method is that reported usage is not necessarily consumed by patients but rather is an approximation based on the pharmacy distributions. Stock returns to pharmacy are captured as negative quantities and incorporated in published NAUSP usage rates, but other pharmacy departments in South Australia do not routinely record expired stock. These results illustrate that smaller, more remote hospitals have a more substantial proportion of dispensed stock lost due to expiry with 10.6\% of usage in peer Group D and Very Small Hospitals accounting for replacement of expired stock, and 6.0\% in peer Group C hospitals.

Agents that are classified as Contain in the PAL are generally low usage, restricted, antimicrobials. As a proportion of total hospital usage, some Group C hospitals included in National Antimicrobial Utilisation Surveillance Program: 2019 Key Findings\textsuperscript{8} reported a higher proportionate rate of Contain usage in their hospitals compared to some much larger, higher acuity hospitals. Although the actual usage rates of these agents is low, if the stock lost to expiry is accounted for, this study illustrates that a high proportion of these Contain agents may not be used in very remote sites.

Figure 2  Antimicrobial usage rate by AIHW peer group 2018–2020 (3-month moving average). DDD = defined daily dose.
Management of antimicrobial stock in remote locations is challenging; it is essential that appropriate antimicrobials are available when they are required for a patient to ensure optimal patient outcomes and avoid an inappropriate alternative being used. However, given the low patient numbers in some hospitals (e.g., Karoonda hospital has an average monthly OBD count of 17, equating to less than one patient per day), maintaining a stock holding of all antimicrobials is not practical. While inventory management helps to reduce the amount of stock lost to expiry, travelling to retrieve and replace stock can typically be more costly and time-consuming for small hospitals than leaving stock to expire. For the RMCLHN, the cost required to re-distribute stock may exceed the average annual cost of $8,790 lost to expiry. Therefore, ensuring antimicrobials are available must be balanced with a risk that the drug is not used and may expire. Considering the impact of expired stock when interpreting usage rates can lead to a more meaningful analysis of antimicrobial usage and stock management for smaller, more remote hospitals. Such consideration can also lead to more informed decisions from policy makers regarding antimicrobial stewardship in smaller hospitals.

The small hospitals included in this study displayed significant variability in monthly patient activity data over the three-year period. This study relied on the manual entry of expired stock into iPharmacy (Dedalus Global, Milan, Lombardy, Italy), which potentially could be subject to human error. While this may explain some variability in the data, prior literature supports the notion that hospitals with low admission rates are likely to experience wider fluctuation in demand. It was noted that 2020 patient activity data across the RMCLHN healthcare facilities was markedly lower than 2018 and 2019. This decline may be in part due to COVID-19, with numerous restrictions on hospital services and associated measures across all healthcare services to support social distancing contributing to an overall reduction in hospital activity across Australia. The uncertainty regarding anticipated hospital activity at the onset of the COVID-19 pandemic may also have contributed to an increased level of expired stock.

Quantitative surveillance of antimicrobial usage in small sites is challenging due to small patient numbers and limitations with regard to identifying changes over time, however it is a crude method to identify outlying prescribing behaviour to target audits. There is no lower limit in hospital size for contributing data to NAUSP, allowing any hospital to utilise the reporting functionality for stewardship purposes, but very small Group D hospitals are not included in the national aggregate reports.

Another limitation of this study is that the WHO-assigned unit of measure of DDD does not necessarily correspond to a recommended or typically prescribed dose, nor does it account for variations in renal or hepatic function. The WHO does not routinely assign DDD values for topical formulations, therefore topical agents were not included in the usage rates calculated nor the DDD count, but they were included in the cost calculations.

In the future, as more Australian hospitals adopt electronic prescribing, this will enable further understanding of what antimicrobials are consumed at the patient level. With a better understanding of antimicrobial consumption, some of the challenges associated with antimicrobial surveillance in smaller, more remote facilities, as previously discussed, can be addressed.

CONCLUSION

This study provides further insight into the interpretation of antimicrobial usage rates in smaller, remote hospitals and illustrates the logistic and economic challenges of stock management in rural locations. The results demonstrate that expired stock can have a considerable impact on reported antimicrobial usage rates among smaller, more remote hospitals, and consideration of expired stock when interpreting antimicrobial usage rates can allow for more meaningful analysis. This study also provides some explanation of the recent trends in antimicrobial prescribing among smaller healthcare facilities, particularly with usage of restricted agents increasing. Further research could expand this study outside South Australia and determine whether the results of this study reflect the situation for other regional, rural, and remote hospitals in other states and territories.

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CONFLICTS OF INTEREST STATEMENT

The authors have no conflicts of interest to declare.
AUTHORSHIP STATEMENT

All authors meet the requirements for authorship.

ETHICS STATEMENT

Data collected for the purpose of this study was non-identifiable and involved negligible risk, therefore met the conditions for exemption from ethical review.

DATA AVAILABILITY STATEMENT

Raw data were generated from SA Health (Adelaide) dispensing software. Derived data supporting the findings of this study are available from the corresponding author on request.

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