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# A kaleidoscope of antibiotic use in Sri Lanka: are we doing it right?

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## Abstract

Effective antibiotics are essential for both prevention and treatment of infections, and to reduce mortality associated with severe infections. The association between antibiotic use and the development of antibacterial resistance (ABR) is well documented and results in longer illnesses, prolonged hospital stay, increased overall costs and higher mortality. Alert to this crisis, the World Health Assembly adopted a global action plan to combat anti-microbial resistance.

The development of ABR is dependent on prescribing and dispensing practices, the use and misuse of antibiotics by patients, and issues related to the availability and quality of medicines which may drive the use of broad-spectrum antibiotics.

The factors affecting the correct use of antibiotics by different stakeholders are the focus of this oration. The research spans a decade of work in this area and explores the perceptions of the public regarding antibiotics and their use to identify the gaps in perceptions and practices and analyses prescriber practices when treating common infections in patients with and without cancers and the appropriateness of prescribed antibiotics to these patients, especially when prescribed in accordance with National Guidelines. The findings of the first national survey on antibiotic consumption (ABC) are also presented and the work highlights the issues that affect the correct estimation of antibiotic consumption. A low-cost method that can be applied to compare the quality of parenteral antibiotics in vivo is also described.

This information will help identify the areas that need to be addressed to combat the ever increasing threat of antibiotic resistance.


## Introduction

Infectious diseases caused by microorganisms are a global problem. In 2019, global deaths due to common bacterial infections accounted for 7.7 million.[1] Second only to ischaemic heart disease as the leading cause of death, this highlights why reducing bacterial infections is a global public health priority. Effective antibiotics are prerequisites for preventing and treating bacterial infections and protecting patients from potentially fatal infections. The increase in bacterial infections has resulted in increased antibacterial consumption (ABC) globally and assuming no policy changes, global ABC in 2030 is expected to be 200% higher than that of 2015.[2]

The association between ABC and the development of antibacterial resistance (ABR) is well documented, and occur within a few years after they are marketed.[3,4] Infections caused by resistant bacteria result in longer illnesses, prolonged hospital stays, increased overall costs and increased mortality.[3,5] It is expected that the estimated 700,000 deaths due to ABR globally in 2014 will rise to 10 million by 2050.[5] Alert to this crisis, in 2015 the World Health Assembly adopted a global action plan (GAP) to combat antimicrobial resistance (AMR).[6] The WHO's GAP for AMR calls for member states to put in place national plans to urgently combat AMR, and in 2017 a national strategic plan for combating antimicrobial resistance in Sri Lanka 2017-2022 (NSP-AMR 2017-2022)[7] was developed. In order to enhance access to antibacterials for the treatment of commonly occurring infections, to ensure their appropriate use and to reduce inappropriate use of broad-spectrum antibiotics, the World Health Organisation (WHO) introduced the Access, Watch, and Reserve (AWaRe) classification of antibacterials as part of the Essential Medicines List

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in 2019 and recommended that 60% of antibiotics used by a country should be from the Access category.[8]

Infections are a leading cause of morbidity and mortality in the public sector healthcare institutions in Sri Lanka, with zoonotic and other bacterial infections (excluding pneumonia) being the 3rd leading cause of death in 2020.[9] The increase of AMR in the country[10,11] is likely to worsen this situation.

The development of ABR depends on the use and misuse of antibiotics by patients, prescribing and dispensing practices, and issues related to the availability and quality of antibiotics which may drive the use of broad-spectrum antibiotics. The work presented in this oration spans over a decade of exploring some of these aspects in Sri Lanka.

## Public perception and use of antibiotics

The WHO Global Strategy for Containment of Antimicrobial Resistance identifies four patient-related factors that contribute to antibiotic resistance: patients' misperceptions, self-medication, poor adherence to prescribed regimens, and advertising and promotion.[12] As Sri Lanka does not allow direct-to-patient advertising of medicines, we explored the other three aspects.[13]

### *Methods*

In 2012, a cross-sectional survey was carried out in an urban area among 400/464 randomly selected households to explore what people knew about and how they used antibiotics. Data was collected with a validated interviewer-administered questionnaire.

### *Results*

A majority (70.8%) of the study sample knew that antibiotics were "medicines used for infections", their varied perceptions on antibiotics are given in Table 1.

**Table 1. Perception of antibiotics**

| *Perception* | *Percentage* |
|---|---|
| "Germ killers"/ used to treat "infections" | 31.8% |
| "Medicines given for coughs and colds" | 16.8% |
| Given to obtain a rapid recovery from "infections" | 5.8% |
| "Pain killers" | 14.5% |
| "Given for gastritis" | 2.5% |

Only 4.5% correctly stated that antibiotics are "used to treat bacterial infections". More than 2/3rd (69.8%) believed that they needed antibiotics when the illness lasted more than 3 days. 19.8% believed they could select an antibiotic for common infections such as "coughs and colds" and "wounds".

Although 69% believed that the full course of antibiotics should be completed as prescribed only 58.8% had done so. Almost 40% had taken antibiotics until they felt better, while others (1.2%) had not completed the full course due to side effects or allergic reactions. The unused antibiotics were retained by 11.5% for future use.

During the 3 months preceding the study, 37.8% (n=151), had taken antibiotics and 49.7% of them had obtained them without a valid prescription. The majority (76%) had obtained antibiotics without any prescription, 9% by submitting previous prescriptions given for similar illnesses, 9% after showing left-over antibiotics prescribed previously for a "similar illness" and 5% by using a prescription "given to another person for a similar illness". Antibiotics have been taken by 61.7% at some point in their lives without a valid prescription.

Some information regarding antibiotic use was obtained by 62%, and television (44%) and newspapers (25%) were the principal sources of information. Healthcare workers accounted for only 16.5% while 10.5% turned to the internet.

### *Discussion*

Inadequate knowledge of antibiotics and their incorrect use, self-medication and obtaining antibiotics without a prescription are factors that drive the development of ABR.[12] Similar findings on the public's knowledge and use of antibiotics have been found in other studies from Sri Lanka.[14,15] Self-medication too was seen in other studies both locally[16] and globally.[17,18]

Misuse of antibiotics by patients could also be reflective of the prescribing practices of doctors where antibiotics may be prescribed for viral infections. The use of words such as "germs" and "infections" which are general, especially when medical consultation takes place in the vernacular, could contribute towards the lack of specific knowledge about antibiotics and their use.

The failure to complete a full course of treatment contributes to the emergence of resistant bacteria.[6,12] Treatment was not completed by 40% in our study and was this comparable to findings from a WHO multi-

country survey.[19] Laws and restrictions on antibiotic sales have been ineffective in preventing indiscriminate sales in other countries too.[18,20]

## Prescriber adherence to national guidelines and appropriateness of recommended empirical antibiotics

Timely initiation of appropriate antibiotic therapy is essential to improve the outcomes of patients with bacterial infections. As microbiological diagnosis takes 24-72 hours, initial therapy is guided by clinical presentation, national guidelines and in-vitro antibiotic sensitivity patterns according to local epidemiology.[21] Adherence to guidelines is intended to improve the outcome of infectious diseases through early and appropriate antimicrobial therapy while minimizing the emergence of ABR. Significant improvement in length of hospitalization and mortality from infections is seen when clinicians are compliant with antibiotic guidelines.[22,23] Assessment of the extent of physicians' adherence to the national guidelines is important to assess whether national antibiotic stewardship efforts are moving in the right direction.[24]

Infections in cancer patients carry higher mortality compared to those without cancers. The spectrum of bacterial pathogens isolated from cancer patients has changed over the past decades with a shift towards multidrug-resistant bacteria (MDR)[25] and this further increases mortality. While early treatment of infections in these patients is crucial, existing national guidelines do not clearly define empirical antibiotic regimens for MDR bacteria causing infections in non-neutropenic and non-septic cancer patients.[26]

Prospective cross-sectional studies were conducted in a tertiary care hospital[27] and at Apeksha Hospital, Maharagama[28] between June 2018 and March 2019. The objectives were to assess the extent of physicians' adherence to the national guidelines for the prescription of parenteral empirical antibiotics for three common infections – lower respiratory tract infection (LRTI), skin and soft tissue infection (SSTI), and urinary tract infection (UTI) in these two settings, to determine whether the national guidelines reflect the current bacterial susceptibility patterns for selected infections, to determine the appropriateness of the prescribed empirical antibiotics for the selected infections, and to analyse the antibiotics prescribed according to WHO's AWaRe classification.[29] We also wanted to see whether there were differences in causative organisms and prescribed antibiotics in these two populations.

### *Methods*

Bacterial isolates of adults presenting with the selected infections to the study settings and prescribed parenteral empirical antibiotics were included in the study. The isolates were determined to be pathogenic by a microbiologist according to standard procedures. Isolates were re-cultured and the sensitivity of bacterial isolates to recommended and prescribed antibiotics was assessed by disk-diffusion method. Details of empirical antibiotic regimens were extracted from in-patient records.

Adherence to guidelines was defined as prescribing empirical antibiotics concordant with the National Guidelines on the Empirical Use of Antibiotics published by the Sri Lanka College of Microbiologists (SLCM) in 2016.[26] Treatment was considered appropriate if the isolated pathogen(s) was sensitive in vitro to at least one of the antibiotics prescribed empirically. Therapy was considered inappropriate if the isolated bacteria were resistant in vitro to all empirical antibiotics prescribed or when the empirical antibiotic did not have the spectrum of activity against the causative bacteria according to the Sanford Guide.[30]

### *Results*

Bacterial isolates (n=160) obtained from patients without cancers admitted to medical and surgical wards of the tertiary care hospital (n=158) and 155 bacterial isolates from 148 cancer patients with selected infections were the study samples. The mean duration of hospital stay before collection of samples for cultures was longer in cancer patients compared to those without (5.63 days vs 1.88 days), suggesting a possibility of hospital-acquired infections in the former. Analysis and comparison of study samples and bacterial isolates from study sites are given in Table 2.

Majority of isolates in both populations for all three infections were Gram-negative organisms, with ESKAPE and *E. coli* accounting for >90% of isolates. There was no significant difference between the proportions of commonly isolated bacteria between the two populations for respiratory and skin and soft tissue infections. However, *E.coli* was commoner in non-cancer patients with UTI while Enterococcus spp. was significantly higher among cancer patients with UTI.

A higher proportion of MDR organisms was seen in isolates of cancer patients (66.1% vs 40.1%). Statistically significant differences were observed in the proportions of different types of superbugs in cancer patients. The use of broad-spectrum Watch antibiotics was significantly higher in cancer patients.

**Table 2. Analysis of study samples and bacterial isolates**

| | *Non-cancer patients*[27] *n=158* | *Cancer patients*[28] *n=148* | *P value* |
|---|---|---|---|
| *Type of Infection* | | | |
| UTI | 35.4% | 33.8% | |
| LRTI | 33.5% | 37.2% | |
| SSTI | 31% | 29.1% | |
| Polymicrobial infections | 3 (LRTI-2, SSTI-1) | 8 (LRTI-3, SSTI-5) | |
| Mean duration of hospital stay before specimen collection for cultures | 1.88 days (SD=1.3) | 5.63 days (SD=3.01) | |
| | | | |
| *Bacterial isolates* | No of isolates n=160 | No of isolates n=155 | |
| Gram-negative organisms | 86.3% | 80.0% | |
| | | | |
| MDR organisms | 40.6% | 66.1% | *<0.0001 |
| Enterobacteriaceae | 41.8% | 71.3% | *<0.0001 |
| ESBL producing *Enterobacteriaceae* | 24.5% | 20.0% | 0.34 |
| Carbapenem resistant *Enterobacteriaceae* | 8.5% | 41.1% | *<0.0001 |
| Methicillin-resistant *Staph aureus* (MRSA) | 84.6% | 71.4% | *0.0053 |
| MDR in *Acinetobacter* isolates | 100% | 100% | |
| | | | |
| Guideline concordance | 92.4% | 67.5% | *<0.0001 |
| Resistance to empirical antibiotics | 29.5% | 48.4% | *0.0007 |
| Antibiotic did not have the spectrum of activity | 15.1% | 29% | |
| Empirical antibiotic appropriate | 47.5% | 20.6% | *< 0.0001 |
| | | | |
| WHO Watch category antibiotics | 67.1% | 81.5% | *0.0041 |

* statistically significant

***Discussion***

This study compared guideline concordance and appropriateness of empirical treatment for three common infections between patients with and without cancers. To the best of our knowledge, this is the first to do so.

A predominance of Gram-negative bacteria was seen in all three selected infections for both patient populations. The majority of the bacteria isolated in non-cancer patients belonged to the family Enterobacteriaceae (coliforms). Similar findings were observed in several previous studies done in Sri Lanka on urinary tract and lower respiratory tract infections.[31-33] However, compared to a study done in 2009 in the same setting for non-cancer patients,[33] we observed a considerable increase in antibiotic resistance rates among urinary coliforms.

Except for MRSA, the proportions of antibiotic-resistant bacteria isolated from cancer patients in our study are similar to the proportions of resistant bacteria in hospital-acquired infections (HAIs) reported from studies conducted in low- and lower-middle-income countries.[34]

Increasing antimicrobial resistance is a major problem in cancer treatment facilities worldwide[35] and the emergence of ESBL-producing Enterobacteriaceae has become a serious problem for which there are very few treatment alternatives. Carbapenems are the cornerstone of treatment for these organisms but the increased use of carbapenems in empirical therapy has resulted in an increased risk of selecting resistant organisms. Our findings also showed a higher rate of use and resistance to carbapenem in cancer patients (41.1% vs 8.5% in non-cancer patients) which is a problem that needs urgent attention.

ESKAPE bacteria and *E. coli* accounted for 90.8% of isolates in both study settings, and these bacteria have a high potential for developing ABR in immuno-compromised patients.[36] Cancer patients infected with ESKAPE pathogens often receive inappropriate empirical antibiotic therapy[37] and nearly 1/3 of isolates from non-cancer patients and 48.4% of isolates from cancer patients showed resistance to empirical antibiotics prescribed. The observed significantly higher prevalence of MDR bacteria in cancer patients underscores the need for separate guidelines for the treatment of infections in such patient populations.

Good adherence to national guidelines (92.4% in non-cancer and 67.5% in cancer patients) augurs well for the antibiotic stewardship programme of the country. Despite this, only 56.1% of non-cancer patients and an alarming 20.6% of cancer patients had received appropriate antibiotic therapy where the prescribed antibiotic had the correct spectrum of activity, and the isolate was susceptible to it. To capitalize on good adherence to national guidelines, these should be updated regularly to reflect the changing sensitivity patterns of bacteria with special provisions for patients with cancers who are more likely to have MDR organisms. There is consistent evidence that guidelines on empirical antibiotic use do not routinely consider current resistance patterns in their recommendations.[38] Considering the prevailing resistance patterns when antibiotic guidelines are developed will therefore result in more patients getting effective antibiotics as well as prevent overuse of "Watch" and "Reserve" antibiotics. Failure to do so would cause treatment failures leading to a loss of confidence in such guidelines and prescribers resorting to the prescription of more potent broad-spectrum antibiotics resulting in the development of resistance to such antibiotics.

Severe infections must be treated with broad-spectrum empirical antibiotics to cover the likely causative organisms and the parenteral antibiotics recommended by the national guideline for such infections are also mostly broad-spectrum[26] and therefore from the Watch group.[29] Despite the national consumption of "Watch" group antibiotics in the public sector for 2017 being 25%,[39] the use of broad-spectrum WHO's Watch group antibiotics was much higher in both of our study sites (67.1% and 81%).[27,28] This difference is likely due to only parenteral antibiotics being considered in our study.

## Antibiotic consumption patterns of health care sectors in Sri Lanka

The WHO defines consumption data as "estimates derived from aggregated data sources such as import or wholesaler data, or aggregated health insurance data where there is no information available on the patients who are receiving the medicines or why they are being used".[40] National antibiotic consumption (ABC) data provides a proxy estimate of the use of antibacterials in a country and reliable ABC data is a prerequisite when planning strategies to combat ABR.

As this information was not available for Sri Lanka, we conducted a descriptive cross-sectional study with aggregate data on ABC for 2017 extracted from all available data sources.[39] Our objectives were to quantify and describe the national ABC in Sri Lanka and to examine any differences in the consumption between public and private sectors. This was the first national survey to analyse data from both these sectors.

### *Methods*

The survey methodology was adapted from WHO methodology for a global programme on surveillance of antimicrobial consumption.[40] Aggregate data on national consumption of systemic antibacterials for 2017 (J01-Anatomical Therapeutic Chemical (ATC) classification) was extracted from all available data sources and classified using ATC classification. The quantity of consumption was converted to Defined Daily Doses (DDDs). Selected key quality indicators of ABC were compared between the public and private sectors.

### *Results*

Data from the Medical Supplies Division (MSD), State Pharmaceuticals Corporation (SPC), State

Pharmaceuticals Manufacturing Corporation (SPMC) and 12 private importers were analysed. Although 78 were registered as private importers with the NMRA, the exact number of companies that actually imported antibacterials in 2017 was not available. Four local manufacturers did not provide data.

The ABC for 2017 was 343.46 million DDDs. Despite most of the inpatient care being provided by the public sector with outpatient care being shared between the public and private sectors, the private sector ABC was 246.76 million DDDs compared to 97.96 million DDDs distributed by the MSD to the entire public sector.

The top four groups of antibacterials consumed in Sri Lanka for 2017 (in ATC groups) were beta-lactams and penicillins, other beta-lactams, macrolides and quinolones. The detailed comparison of ABC (in DDDs) between sectors is given in Figure 1.

The top four most frequently consumed antibiotics in the public sector were amoxicillin, benzylpenicillin, cloxacillin and cefuroxime while it was co-amoxiclav, azithromycin, ciprofloxacin and amoxicillin in the private sector. Benzylpenicillin consumption was exclusively in the public sector. Figure 2 shows the consumption of antibacterials in the "Access, Watch and Reserve" categories for the country and public and private sectors.

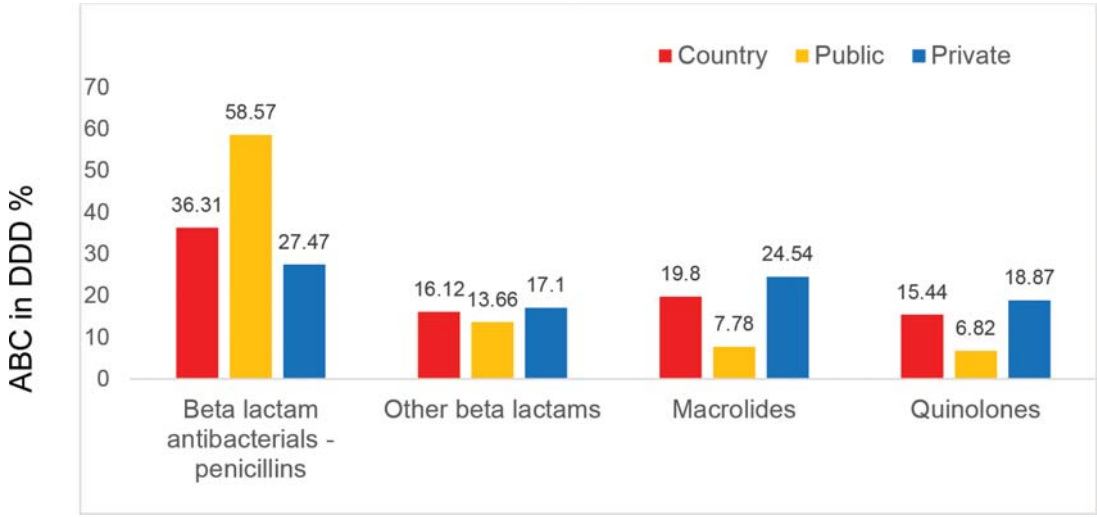


**Figure 1. Commonly consumed antibiotic ATC groups for 2017.**

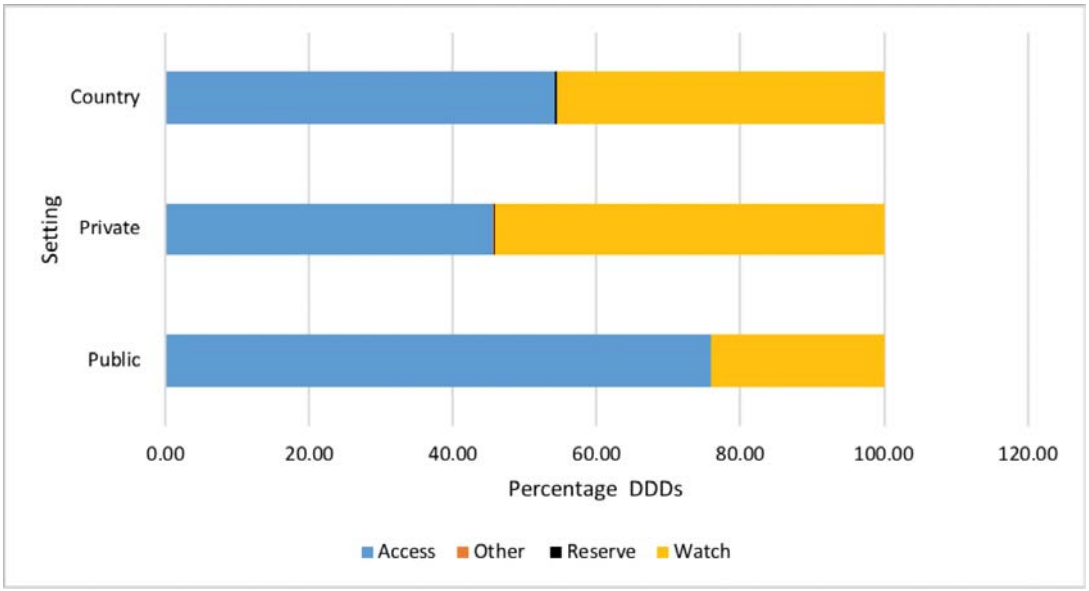


**Figure 2. Consumption of antibacterials in Access, Watch and Reserve categories.**

**Table 3. Comparison of quality indices**

| *Quality Index* | *Public Sector* | *Private Sector* | *Country* |
|---|---|---|---|
| J01CE_%<br>*(Consumption of beta-lactamase sensitive penicillins)* | 18.77 | 0.18 | 5.46 |
| J01CR_%<br>*(Consumption of combination of penicillins)* | 8.98 | 15.83 | 13.89 |
| J01DD+DE_%<br>*(Consumption of third and fourth generation of cephalosporin0s* | 0.72 | 1.98 | 1.62 |
| J01_B/N<br>*(Consumption of fluoroquinolones (J01MA))* | 6.71 | 18.81 | 15.31 |
| J01_B/N<br>*(Broad spectrum penicillins: Narrow spectrum penicillins)* | 0.81 | 5.25 | 2.86 |
| Access-to-Watch Index (AW-I) | 3.16 | 0.84 | 1.18 |

Of the total ABC for Sri Lanka, 54.19% was from the Access category while 45.57% was from the Watch group. However, the consumption of Watch category antibiotics was higher in the private sector (54.11%) compared to that of the public sector (24.11%). The consumption of broad-spectrum, Watch group antibiotics in the private sector was more than the consumption of narrow-spectrum, Access group in the public sector. Consumption of Reserve group antibacterials was negligible and limited to the private sector.

Quality indicators of ABC for the country as a whole and separately for public and private sectors are given in Table 3. Indicators are calculated for total data to show how one sector affects the country data. All quality indices show disproportionately higher use of broad-spectrum antibiotics in the private sector when compared to the public sector.

***Discussion***

Our study showed a higher ABC in the private sector with greater consumption of Watch group antibiotics compared to those from the Access group. The higher ABC of the private sector could be due to the significant proportion of outpatient care provided by the private sector which includes the private hospitals and independent family physicians in the community.

In 2015, the most consumed antibacterial classes globally were broad-spectrum penicillins (J01CA), cephalosporins (J01D), quinolones (J01M) and macrolides (J01F).[1,40] There was also an increase in the consumption of Watch antibiotics. Sri Lanka showed a similar pattern ABC in 2017. Compared to the public sector, all quality indices show disproportionately higher use of broad-spectrum antibiotics in the private sector.

The higher consumption of Watch group antibacterials in the private sector in Sri Lanka is a concern especially as there is no data to suggest that the causative bacteria and/or their antibacterial sensitivity patterns differ between the sectors. This is more alarming as there is an increasing emergence of multidrug-resistant bacteria in the country.[41-43] The freedom to prescribe any medicine that is available in the country and the better financial status of patients who seek treatment from the private sector could contribute to the greater use of broad-spectrum and newer antibacterials in the private sector. The increased use of “Watch” antibiotics could also be because the prescribers have noticed poor responses to “Access” antibiotics in their practices.

An important limitation of our study was the inability to capture all national data. This was largely due to incomplete and inadequate record-keeping by the Customs and private importers. The SPMC was unable to provide consumption data based on the sector to which it supplied.

## Comparison of in vitro efficacy of different brands of parenteral antibiotics

Sri Lanka has the lowest GDP-adjusted price for medication in the SAARC region for several selected drugs, including parenteral antibiotics.[44] Generic drugs reduce healthcare expenditure and are expected to be similar in efficacy and safety to the innovator. However, low-efficacy generic antibiotics are available, resulting in therapeutic failures[45,46] and the development of ABR.[47] The perception among prescribers that generic products or what is available in public hospitals are of a lower efficacy drives the selection of antibiotics with a broader spectrum to treat infections. This is especially so for injectable antibiotics, where the WHO does not recommend bioequivalence testing for parenteral generic antibiotics before they are registered. This perception may lead to prescribers requesting an expensive brand of the same antibiotic or prescribing an antibiotic with a broader spectrum of activity, especially as these are to treat severe infections.

We compared the in vitro efficacy[48,49] of five different parenteral antibiotics available in the public healthcare system (MSD) along with two other products of the same antibiotic with the highest sales in the Sri Lankan pharmaceutical market for 2018/2019 based on sales data obtained from IQVIA Sri Lanka.

### Methods

The antibiotics were reconstituted according to the manufacturer's instructions. Serial dilutions for microbiological assay were prepared with these solutions. Minimum Inhibitory Concentration (MIC) and Minimum Bactericidal Concentration (MBC) were determined according to Clinical and Laboratory Standard Institute (CLSI) guidelines. Three brands each of meropenem, ceftazidime, ceftriaxone, ciprofloxacin, and vancomycin were tested against sensitive clinical isolates obtained from patients with LRTIs, SSTIs or UTIs and standard bacterial strains (*E. coli* ATCC® 25922, *P. aeruginosa* ATCC® 27853, and *S. aureus* ATCC® 29213). Four of the selected antibiotics were among the most prescribed antibiotics in our previous studies and vancomycin was selected as it is an antibiotic effective against MRSA, which was a common MDR bacteria identified.[27,28] All 5 antibiotics were from the WHO's Watch group[29] and have a broad spectrum of activity.

### *Results*

Comparisons of average MICs and MBCs of the selected parenteral antibiotic brands against test bacterial isolates are given in Figures 3 and 4 respectively.[49]

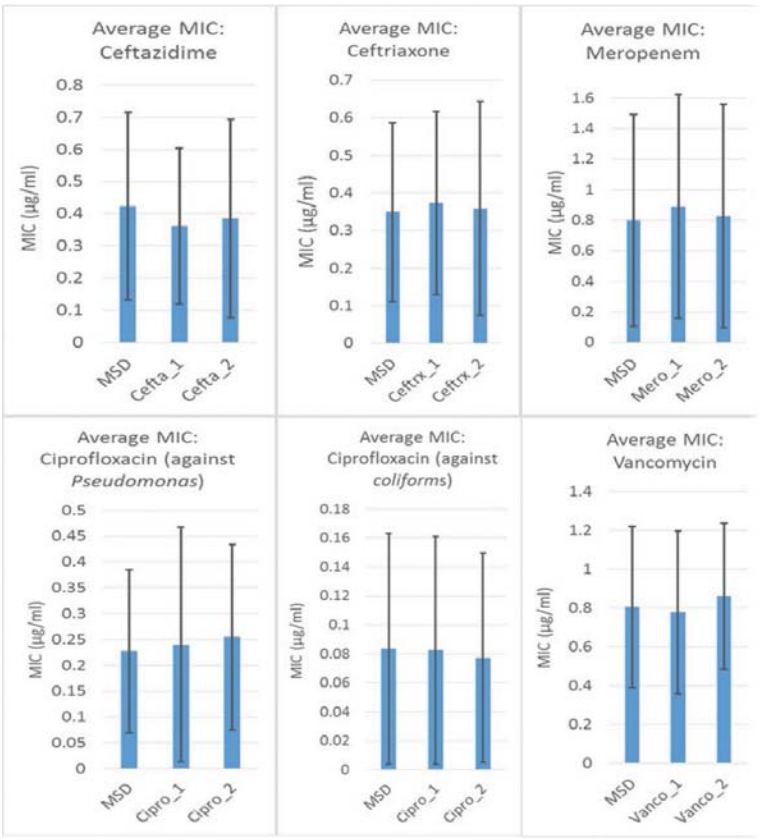


**Figure 3. Comparison of average MICs of the selected parenteral antibiotics against test bacterial isolates.**[49]

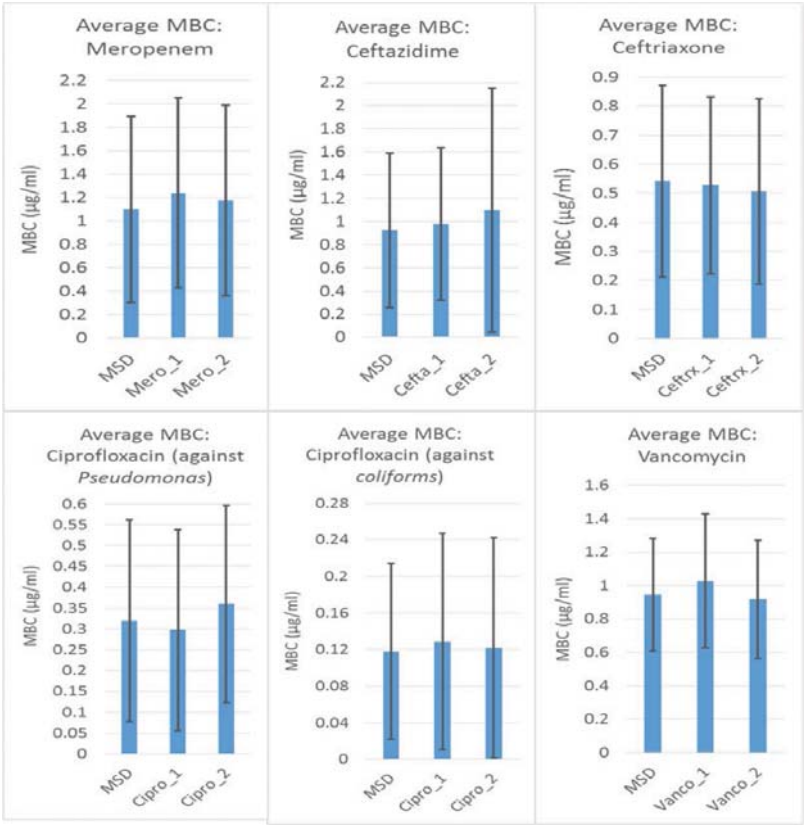


**Figure 4. Comparison of average MBC of the selected parenteral antibiotics against test bacterial isolates.**[49]

All evaluated products showed sufficient inhibitory activity as the MIC values for the standard strains were found to be in the CLSI recommended range and behaved similarly in vitro as the MICs and the MBCs did not have significant differences for the tested clinical isolates.

## Discussion

Our results showed a comparable in vitro antibacterial activity for parenteral antibiotics available in the public health sector and those with the highest sales in the pharmaceutical market. Similar results have been seen in other studies done globally which evaluated different brands of meropenem,[50] vancomycin,[51] ceftriaxone,[52,53] ciprofloxacin,[54] and ceftazidime.[55] However, there have been instances where generics have shown a lower efficacy than the innovator.[56,57]

Pharmacokinetics of the antibiotics and patient factors such as comorbid illnesses will also affect the clinical response to antibiotics.[50,56,58,59] This complicates the quality assessment of generic antibiotics as no single tool exists for evaluating all quality aspects.[56]

## Conclusions

The work presented shows that the public misuses antibiotics, and alarmingly, think that they know what they are doing and worse, that they are right. It shows that laws and regulations have been ineffective, and anyone can buy antibiotics from a pharmacy without a valid prescription, even today.

It also shows that prescriber practices should be reviewed and that they should play a bigger role in educating the public. It highlights the need to use general terms like “germs” and “infections” carefully, especially in the vernacular, as they may give the wrong message.

Our work has shown that being concordant with guidelines may not necessarily result in appropriate empirical treatment. It also showed that antibiotic prescribing based on experience is no better. To capitalize on good guideline concordance by prescribers, the guidelines should be updated regularly in keeping with the rapidly changing AMR patterns.

As a country, we use more broad-spectrum antibiotics than we should and we are at a greater risk

of ABR and the development of MDR strains. The significant use of Watch group antibiotics in the private sector needs further exploration, especially as the prescribers and more importantly, the organisms, are the same in both sectors. The work also highlights the need for accurate and complete record-keeping for proper ABC surveillance.

We have shown that relatively inexpensive methods are available to simultaneously evaluate multiple antimicrobial agents for potency, especially as a screening tool. The MBC can be used to evaluate formulations, specifically when contamination is suspected.

Our work, however, leaves important questions unanswered: If the potency of the brands is the same, why do clinicians feel that what they have in public hospitals is ineffective? Are there issues in the transport or storage that can affect the efficacy? Are there patient-related factors that we do not actively consider that can affect outcomes? These are areas for further research.

The development of new antibiotics is expensive and time-consuming. The complete development of a typical broad-spectrum antibiotic (i.e. from discovery to market) may take on average 13-14 years and will cost anything between 150-600 million Euros, excluding the extended costs for failed molecules and the lost opportunities associated with increased cycle time.[60] It is therefore not surprising that there has been no development of new classes of antibiotics for the last 40 years.[61]

If AMR continues unchecked, in less than 3 decades global deaths from infections due to resistant bacteria will reach a staggering 10 million a year.[62] Low-Income Countries (LICs) and Lower-Middle-Income Countries (LMICs) bear a significant burden of infectious disease. South Asia is forecasted to be one of the super-regions for bacterial AMR deaths and these deaths will be more in those 70 years and older.[62] Every one of us here today, will be among those statistics.

Rational ABC and combatting ABR should not be the prerogative of one group or an entity. The Ministry of Health should provide leadership and act as the National Focal Point to combat AMR but should obtain the services of relevant experts. Activities related to ABR are not the sole property nor the responsibility of microbiologists or infectious disease specialists; antibiotics are prescribed by everyone in all clinical specialities. These stakeholders must work together with pharmacists and the public to ensure that antibiotics are used correctly. Working together is the only way we can prevent living in the pre-penicillin era, where every scratch could potentially kill.

## Ethical approval

Ethical approval for Studies 1,2,3 and 5 was obtained from the Research Ethics Committee (REC) of the Faculty of Medical Sciences, University of Sri Jayewardenepura. Study 4 was exempted from review by the REC of the Sri Lanka Medical Association.

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