Antimicrobial Stewardship for Neonates

Gayana Gunaratna

Neonates are uniquely vulnerable to infection and frequently exposed to broad-spectrum antibiotics, yet data on resistance patterns are limited, and appropriate empiric therapy remains unconfirmed in many settings

- Antimicrobial resistance is a key factor that determines outcome in neonatal sepsis

- Increasing antimicrobial resistance is directly linked with intense use of antimicrobials

- This has led to the development of an antimicrobial stewardship programme
  - aimed at the rational use of antimicrobials

- Neonates and children are prescribed antimicrobials very frequently
  - exhibit different AMR patterns compared with other age groups

Antimicrobial stewardship programme

Has proved successful in reducing antimicrobial use without negatively affecting neonatal mortality

AMS programmes will help;

- To promote rational use of antimicrobials in healthcare institutions
- To optimize clinical outcomes in the management of infections
- To minimize the unintended consequences of antimicrobial therapy, including toxicity and allergies
- To preserve existing antimicrobials for future use by reducing the development of AMR
- To reduce healthcare costs without compromising the quality of medical care

- There has been progress in the implementation of AMS activities in well-resourced settings
- AMS remains rudimentary in many resource-limited settings
- Traditional AMS approaches have evolved in the context of clearly structured and regulated healthcare systems, with high initial and ongoing costs

Antimicrobial stewardship teams should conduct regular antibiotic rounds at predetermined intervals, depending on the feasibility of a particular institution.

- The core questions addressed by AMS include:

Who should be treated when (indication) with what (drug) and how (dose, duration, and route)

Timely antibiotic management **Who? When?**	- Prompt initiation of AM therapy if bacterial infection suspected - Avoid using AMs when not indicated (eg, upper respiratory tract infection) - Inclusion of guidance on clinical syndromes that do and do not require AM therapy in clinical guidelines and algorithms

Appropriate selection of antibiotics

What?

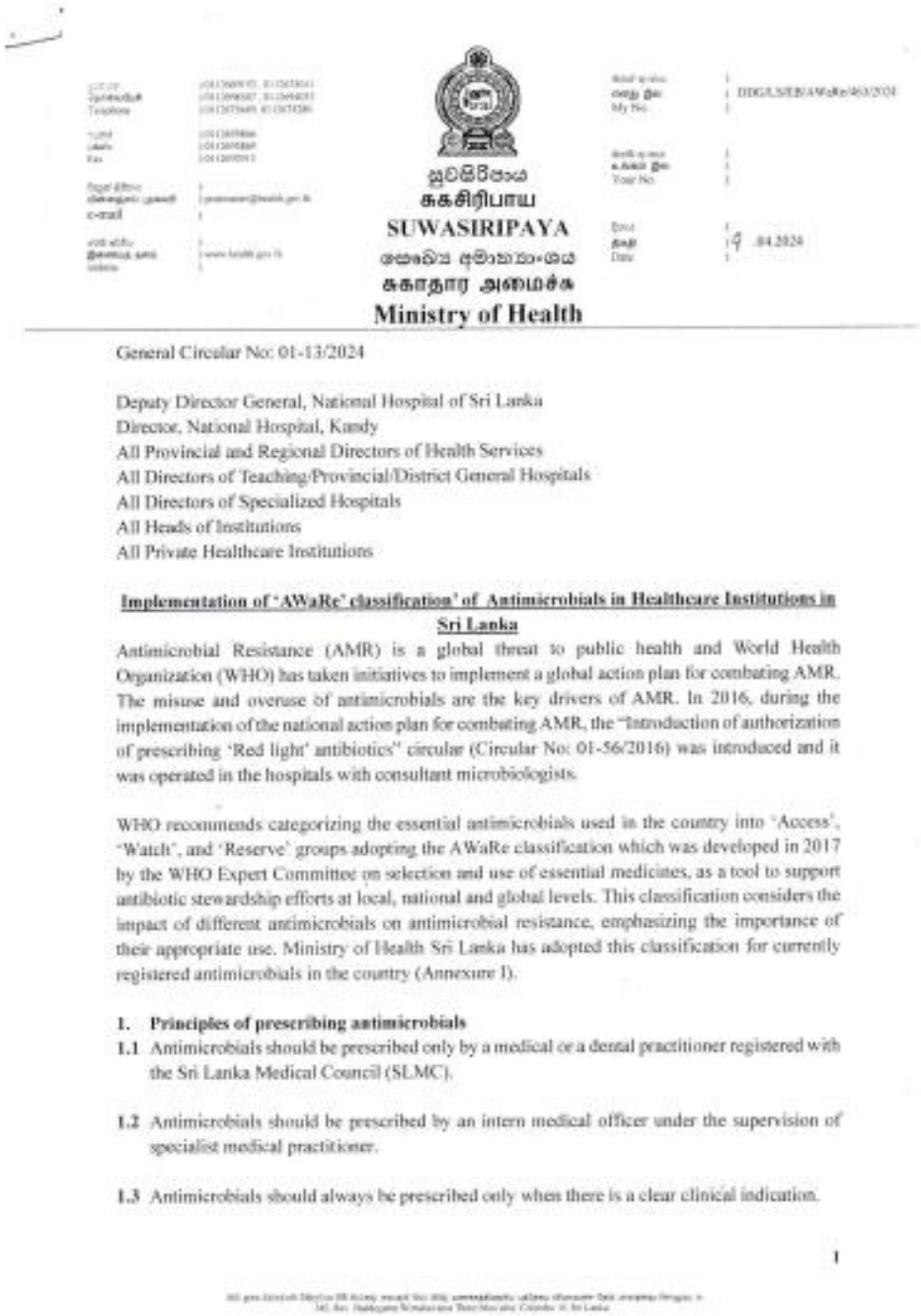
- Selection of appropriate AM regimens
- Selection of AMs on basis of local antibiograms and guidelines with preference given to AMs less likely to promote the emergence of resistance

Appropriate administration and de-escalation of antibiotics	- Optimize dosing (ie, never use "low dose")
How?	- Review microbiology and clinical status at 48–72 h to decide: stop, switch, continue, modify
	- Administer short antibiotic courses as appropriate
	- Therapeutic drug monitoring
	- Appropriate prophylactic use of AMs

	use of AMS
Use of expertise and resources **Resources**	- Establishment of AS teams/committees and identification of AS champions - Administrative and leadership support - Collaboration with manufacturers

Continuous and transparent monitoring of antibiotic use and antimicrobial resistance	- Audit and feedback - Education - Prospective monitoring of relevant outcomes - Benchmarking

Information



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சுகசிரிபாய
SUWASIRIPAYA
சுகாதார அமைச்சு
Ministry of Health

General Circular No: 01-13/2024

Deputy Director General, National Hospital of Sri Lanka
Director, National Hospital, Kandy
All Provincial and Regional Directors of Health Services
All Directors of Teaching/Provincial/District General Hospitals
All Directors of Specialized Hospitals
All Heads of Institutions
All Private Healthcare Institutions

Implementation of 'AWaRe' classification' of Antimicrobials in Healthcare Institutions in Sri Lanka

Antimicrobial Resistance (AMR) is a global threat to public health and World Health Organization (WHO) has taken initiatives to implement a global action plan for combating AMR. The misuse and overuse of antimicrobials are the key drivers of AMR. In 2016, during the implementation of the national action plan for combating AMR, the "Introduction of authorization of prescribing 'Red light' antibiotics" circular (Circular No: 01-56/2016) was introduced and it was operated in the hospitals with consultant microbiologists.

WHO recommends categorizing the essential antimicrobials used in the country into 'Access', 'Watch', and 'Reserve' groups adopting the AWaRe classification which was developed in 2017 by the WHO Expert Committee on selection and use of essential medicines, as a tool to support antibiotic stewardship efforts at local, national and global levels. This classification considers the impact of different antimicrobials on antimicrobial resistance, emphasizing the importance of their appropriate use. Ministry of Health Sri Lanka has adopted this classification for currently registered antimicrobials in the country (Annexure I).

1. **Principles of prescribing antimicrobials**

1.1 Antimicrobials should be prescribed only by a medical or a dental practitioner registered with the Sri Lanka Medical Council (SLMC).

1.2 Antimicrobials should be prescribed by an intern medical officer under the supervision of specialist medical practitioner.

1.3 Antimicrobials should always be prescribed only when there is a clear clinical indication.

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Implementation of 'AWaRe' classification of Antimicrobials in Healthcare Institutions in Sri Lanka

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- WHO recommends categorizing the essential antimicrobials used in the country into Access', Watch', and 'Reserve' groups, adopting the AWaRe classification, which was developed in 2017

- Is considered a tool to support antibiotic stewardship efforts at local, national, and global levels.

- This classification considers;
  - the impact of different antimicrobials on antimicrobial resistance
  - the importance of their appropriate use

- The Ministry of Health, Sri Lanka, has adopted this classification for currently registered antimicrobials in the country

Any patient who is prescribed antimicrobials should be reviewed after 48-72 hours to assess the need for continuation or de-escalation of antimicrobial therapy based on the results of the investigations using the Antimicrobial Prescription Chart

'Access' antimicrobials

Should be prescribed according to standard treatment guidelines by a Medical or a Dental practitioner registered in the Sri Lanka Medical Council (SLMC)

Access
Antimicrobials
Amoxicillin
Amoxicillin/clavulanic-acid
Ampicillin
Benzathine-benzylpenicillin
Benzylpenicillin
Cefalexin
Cefazolin
Cefuroxime
Clarithromycin
Clindamycin
Cloxacillin
Doxycycline
Erythromycin
Flucloxacillin
Gentamicin
Metronidazole
Nitrofurantoin
Norfloxacin
Ornidazole
Phenoxymethylpenicillin
Procaine-benzylpenicillin
Sulfamethoxazole/trimethoprim
Tetracycline
Tinidazole
Trimethoprim

Anti-Fungal
Griseofulvin

Anti-Viral
Acyclovir (Oral)

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- 'Access' antimicrobials have
  - a narrow spectrum of activity
  - a lower cost
  - a good safety profile

- They are often recommended as empiric first or second-choice treatment
- They offer the best therapeutic value
- They have a minimal potential for developing and inducing resistance
- These drugs should be widely available.

'Watch' antimicrobials

Should be prescribed only under the guidance of a specialist medical practitioner.

Watch
Amikacin
Azithromycin
Cefixime
Cefotaxime
Ceftazidime
Ceftriaxone
Chloramphenicol
Ciprofloxacin
Ertapenem
Imipenem/cilastatin
Mecillinam
Meropenem
Netilmicin
Ofloxacin
Piperacillin/tazobactam
Pivmecillinam
Rifamycin
Rifaximin
Roxithromycin
Secnidazole
Spectinomycin
Spiramycin
Streptomycin
Sulfadiazine
Sulfadiazine/trimethoprim
Teicoplanin
Vancomycin

Fluconazole
Itraconazole
Terbinafine

Acyclovir IV
Oseltamivir
Valganciclovir Oral

They have more potential for developing and inducing resistance

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'Watch' antimicrobials:

- The first or second choice of antimicrobials only indicated for a specific, limited number of infective syndromes

- Should be reviewed by the Consultant Microbiologist/ treating Specialist Medical Practitioner within 48-72 hours

- If an alternative antimicrobial belonging to the 'Watch' group has to be started at the primary care level instead of the primary treatment option of the guideline, a clear indication with justification has to be documented

'Reserve' antimicrobials

Should be discussed with the Consultant Microbiologist of the hospital before prescribing

Reserve
Ampicillin/sulbactam
Aztreonam
Ceftazidime/avibactam
Cefepime
Cefoperazone/sulbactam
Colistin
Daptomycin
Fosfomycin
Fusidic acid
Levofloxacin
Linezolid
Minocycline
Moxifloxacin
Polymyxin-B
Rifampicin
Tigecycline

Amphotericin B
Anidulafungin
Caspofungin
Flucytosine
Posaconazole
Voriconazole

Cidofovir
Foscarnet
Ganciclovir IV
Ribavirin IV

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'Reserve' antimicrobials:

- Includes last resort antimicrobials
- Should only be used in highly selected infections

  Eg; Life-threatening infections due to MDR organisms
- Use should be tailored to highly specific patients and settings

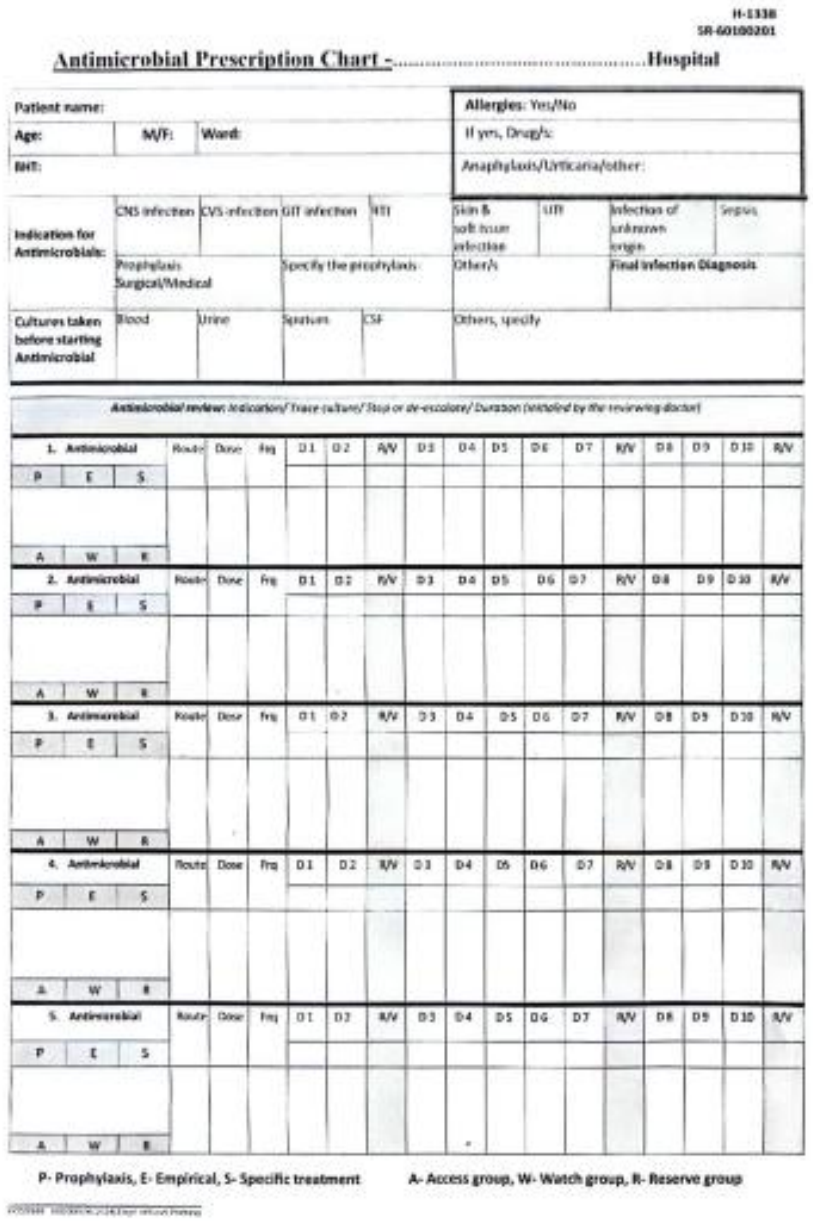
  - when all alternatives have failed or are not suitable
- Are key targets of national stewardship programmes,

  - need monitoring and utilization reporting

If a 'Reserve' group antimicrobial is required to start urgently, any mode of communication is permitted for discussion.

Any prescription of a 'Reserve' antimicrobial should be followed by written authorization by the Consultant Microbiologist on the request of treating Specialist Medical Practitioner within three (03) days.

There are no restrictions to prescribe antimicrobials according to the national guidelines.



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Antimicrobial Prescription Chart -.....Hospital

Patient name:					Allergies: Yes/No				
Age:	M/F:	Ward:			If yes, Drug/s:				
BHT:					Anaphylaxis/Urticaria/other:				
Indication for Antimicrobials:	CNS infection	CVS infection	GIT infection	RTI	Skin & soft tissue infection	UTI	Infection of unknown origin	Sepsis	
	Prophylaxis Surgical/Medical		Specify the prophylaxis		Other/s		Final Infection Diagnosis		
Cultures taken before starting Antimicrobial	Blood	Urine	Sputum	CSF	Others, specify				

Antimicrobial review: Indication/ Trace culture/ Stop or de-escalate/ Duration (entered by the reviewing doctor)

	Route	Dose	Freq	D1	D2	R/V	D3	D4	D5	D6	D7	R/V	D8	D9	D10	R/V
1. Antimicrobial																
P E S																
A W R																
2. Antimicrobial																
P E S																
A W R																
3. Antimicrobial																
P E S																
A W R																
4. Antimicrobial																
P E S																
A W R																
5. Antimicrobial																
P E S																
A W R																

P- Prophylaxis, E- Empirical, S- Specific treatment A- Access group, W- Watch group, R- Reserve group

Attach an antimicrobial prescription chart to BHT of all patients who are prescribed antimicrobials, and all entries of antimicrobials should be made on this chart

High Rates of "Watch" and "Reserve" Class Antibiotics Used to Treat Infections in Neonates and Infants in Southeast Asia

Michelle L. Harrison, MPH,† Benjamin F. R. Dickson, MBBS,*† Maria Esterlita T. Villanueva-Uy, MD,‡§ Nina Dwi Putri, MD,¶‖ Riyadi Adrizain, MD,**†† Leny Kartina, MD,‡‡§§¶¶ Gayana P. S. Gunaratna, MD,‖‖***††† Nambage Shirani Chandrasiri, MD,***††† Hoang T. Tran, PhD,‡‡‡§§§ Huong X. Nguyen, PhD,¶¶¶ Siew M. Fong, MBBS,‖‖‖ Erena S. Kasahara, MD,§ Chau H. M. Le, MD,‡‡‡§§§ Distyayu Soekardja, MD,¶ Dominicus Husada, MD,‡‡ Ng Boon Hong, MD,‖‖‖ and Phoebe C. M. Williams, DPhil,*†*****

Abstract: We evaluated antibiotic prescribing practices for neonates and infants hospitalized with infections in resource-constrained healthcare settings, where antimicrobial resistance is responsible for significant neonatal morbidity and mortality. A point prevalence survey of 667 admitted infants across 10 clinical sites in Southeast Asia revealed a total of 405 antibiotics were prescribed to 218 infants, with high use of World Health Organization-classified "Watch," "Reserve" and "Not Recommended" antibiotics.

Key Words: antimicrobial resistance, antimicrobial stewardship, neonatal infection, neonatal sepsis, AWaRe

(*Pediatr Infect Dis J* 2025;44:e113–e116)

Antimicrobial resistance is a major public health challenge, and the increasing burden of multidrug-resistant infections in children is of particular concern. As more babies are born in

implementing infection prevention and control strategies can propagate the spread of MDR bacteria.

In an effort to slow the selection pressure driven by antimicrobial overuse and misuse, which may contribute to the rising prevalence of MDR bacteria, the World Health Organization (WHO) recently developed an adjunct to the Essential Medicines List: classifying antibiotics into 3 groups – "Access," "Watch" and "Reserve."[2] The WHO established an overarching goal of 60% of antimicrobial prescriptions being from the "Access" category,[2] yet this target has been difficult to attain; particularly in regions where the prevalence of infectious due to MDR bacteria is greatest, including Southeast Asia.

To adequately understand the challenges associated with meeting antimicrobial stewardship targets, a comprehensive understanding of empirical antimicrobial prescribing practices is essential.

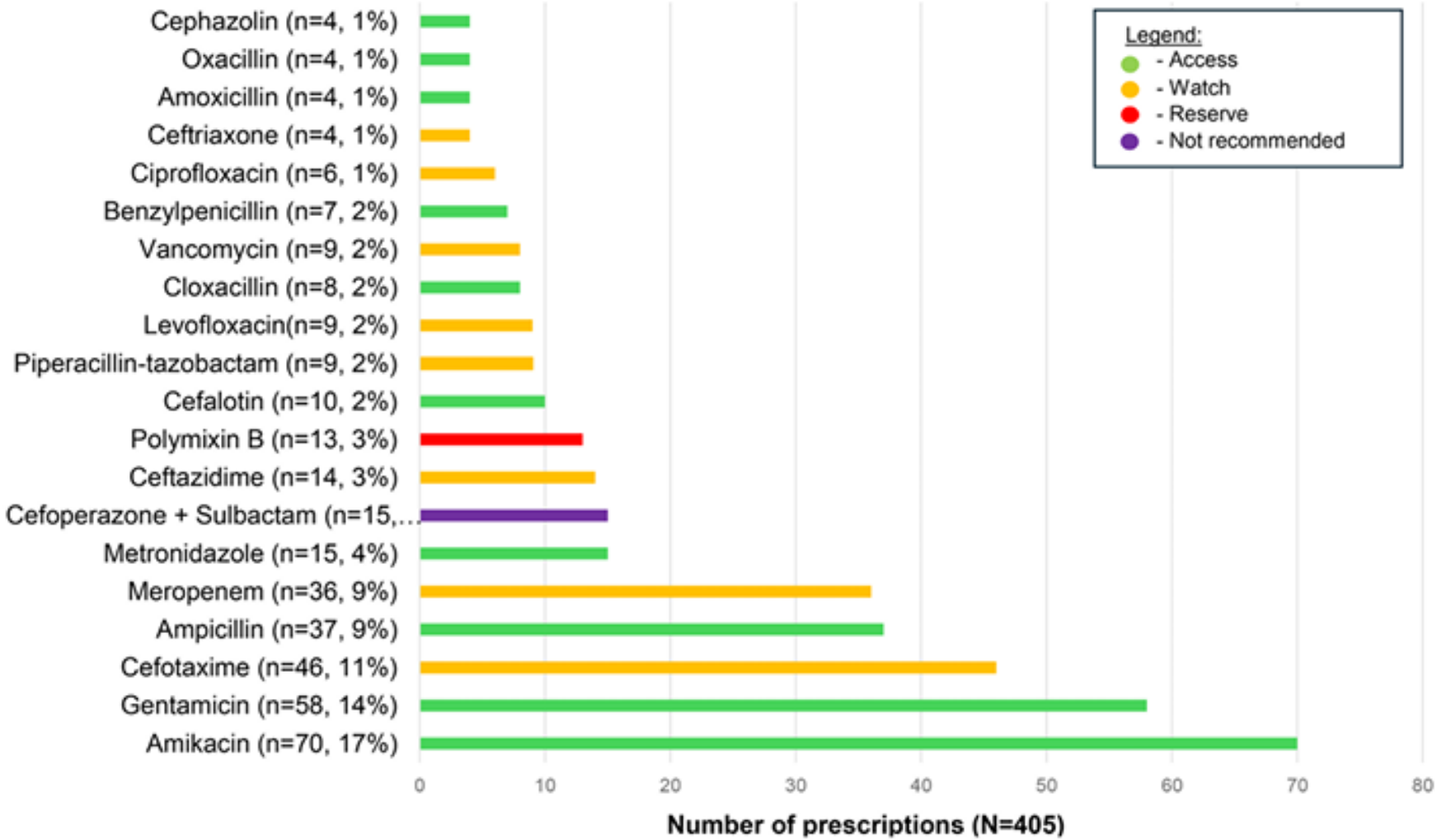

FIGURE 1. Pooled frequency of the most common antibiotics prescribed to treat infections in neonates and infants across 10 clinical sites in Southeast Asia. Note: prescriptions encompassing <1% of the total have been omitted from this graph. full color online

BMJ Paediatrics Open

Antibiotic prescribing in neonatal sepsis: an Australian nationwide survey

Brendan McMullan ,[1,2,3] Celia Cooper,[4] Naomi Spotswood,[5,6,7] Rodney James,[8] Cheryl Jones,[9,10,11] Pamela Konecny,[12,13] Christopher Blyth,[14,15,16,17] Thursky Karen[2,18]

To cite: McMullan B, Cooper C, Spotswood N, *et al*. Antibiotic prescribing in neonatal sepsis: an Australian nationwide survey. *BMJ Paediatrics Open* 2020;**4**:e000643. doi:10.1136/bmjpo-2020-000643

► Additional material is published online only. To view

ABSTRACT

Objective To evaluate quality and variation in antibiotic prescribing for neonatal sepsis.

Design We analysed prescribing in hospitalised neonates using the National Antimicrobial Prescribing Survey in Australian neonates from 1 January 2014 to 31 December 2018.

Setting Data from antibiotic point prevalence surveys performed in hospitals, ranging from rural hospitals to

What is known about the subject?

- Neonatal sepsis is an important cause of morbidity and mortality globally.
- There is considerable uncertainty about antibiotic prescribing and optimal regimens to treat neonatal sepsis.
- Current challenges include lack of epidemiological

Table 3 Top 5 antibiotics by frequency prescribed and sepsis type

Antibiotic: all	Prescriptions Total=415, n (%)	Cumulative percentage
Gentamicin	179 (43.1)	43.1
Benzylpenicillin (penicillin G)	144 (34.7)	77.8
Cefotaxime	26 (6.3)	84.1
Ampicillin	18 (4.3)	88.4
Flucloxacillin	13 (3.1)	91.6
Antibiotic: EOS	**Prescriptions Total=245, n (%)**	**Cumulative percentage**
Gentamicin	119 (48.6)	48.6
Benzylpenicillin (penicillin G)	100 (40.8)	89.4
Ampicillin	12 (4.9)	94.3
Amoxicillin	5 (2)	96.3
Benzathine penicillin	3 (1.2)	97.6
Antibiotic: LOS	**Prescriptions Total=100, n (%)**	**Cumulative percentage**
Gentamicin	31 (31)	31
Cefotaxime	18 (18)	49
Benzylpenicillin (penicillin G)	16 (16)	65
Vancomycin	11 (11)	76
Flucloxacillin	10 (10)	86

EOS, early-onset sepsis; LOS, late-onset sepsis.

CONCLUSIONS

In this nationwide survey we have identified substantial variability in dosing of benzylpenicillin and gentamicin, the two most commonly prescribed antibiotics for neonatal sepsis in this study. Only a small minority of neonates treated for sepsis have culture-confirmed infection. Efforts to optimise therapy for treatment of neonatal sepsis and reach consensus for therapy, including understanding prescribing practices and implementing national guidelines, are recommended.

A situational analysis should be performed before implementing the AMS programme to identify the;

- strengths
- weaknesses
- opportunities
- threats in the institution

ONE SIZE DOES NOT FIT ALL

In summary;

- Neonatal sepsis with its associated antimicrobial resistance puts their well-being at risk.

- AMR is a looming threat to the achievement of a single-digit infant mortality rate, particularly in low-income and middle-income countries.

- All attempts must be made to mitigate antimicrobial resistance

- Antimicrobial stewardship has proven to be effective in combating the threat

We kindly invite you to join us for a point prevalence study

Thank You