

Michelle L Harrison^{1,2}, Dr. Erena Kasahara^{3,4}, Julie Caparas^{3,4}, Prof. Maria E. Villanueva-Uy^{3,4}, Dr. Alkim Ozaygen¹, Patrick Cahill¹, Nover Edward Duarte^{3,4}, Jill Hopkins^{5,6}, Dr. Tamalee Roberts^{5,7}, Dr. Yue Wu^{1,2}, Prof. Tom Snelling^{1,2}, Prof. Paul Turner^{5,6}, Prof. H Rogier van Doorn^{5,8} A/Prof. Phoebe CM Williams^{1,2,9}

¹School of Public Health, Faculty of Medicine, The University of Sydney, Sydney, New South Wales, Australia, ²Sydney Infectious Diseases Institute, Sydney Australia, ³Institute of Child Health and Human Development, National Institutes of Health, Manila, PHILIPPINES, ⁴Philippine General Hospital, Manila, PHILIPPINES, ⁵Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, UK, ⁶Cambodia Oxford Medical Research Unit, Angkor Hospital for Children, Cambodia, ⁷Lao- Oxford Mahosot Hospital Wellcome Trust Research Unit, Laos, ⁸Oxford University Clinical Research Unit (OUCRU), Hanoi, Vietnam ⁹University of NSW School of Women and Children's Health, Sydney, Australia

Background:

Neonatal infections cause significant mortality globally, which will be exacerbated by rising multidrug-resistance.¹ Data describing early- and late-onset neonatal infections guide empirical therapy and are predominantly from high-income countries, where pathogen profiles are thought to differ from those identified in resource-constrained settings,^{2,3} impacting the efficacy of prescribed treatment.

Methodology:

We implemented A Clinically Oriented antimicrobial Resistance Surveillance protocol (ACORN2)⁴ to undertake systematic infection surveillance in a 70-bed neonatal intensive care unit (NICU) at Philippine General Hospital (PGH). We enrolled all **infants admitted to the NICU who were administered intravenous (IV) antibiotics with a presumed infection** between November 14 2023-April 30 2025. Analysis was undertaken on all enrolled neonates (< 28 days corrected age).

Aims: We aimed to evaluate the epidemiology of neonatal infections at Philippine General Hospital, Manila.

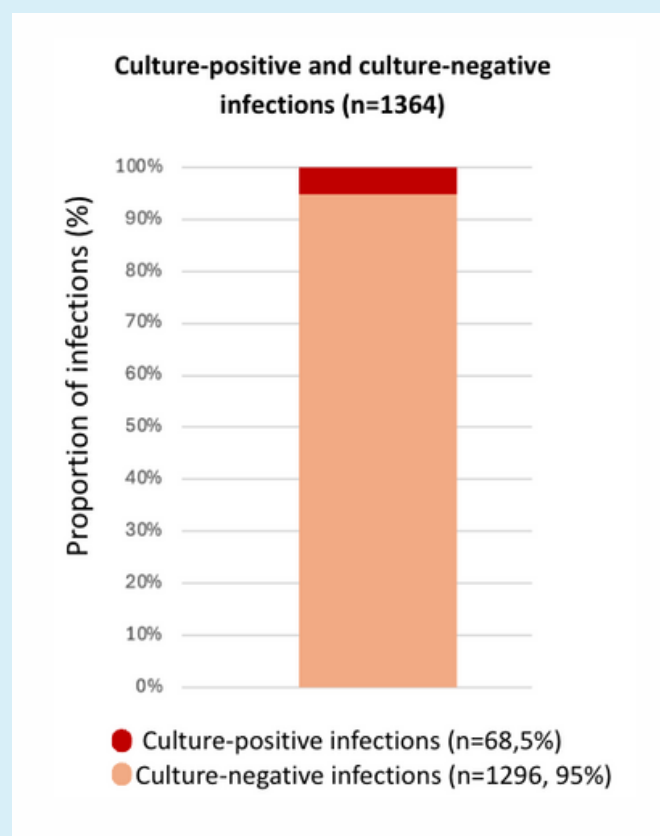


Figure 1. Culture-positive and culture-negative infection episodes

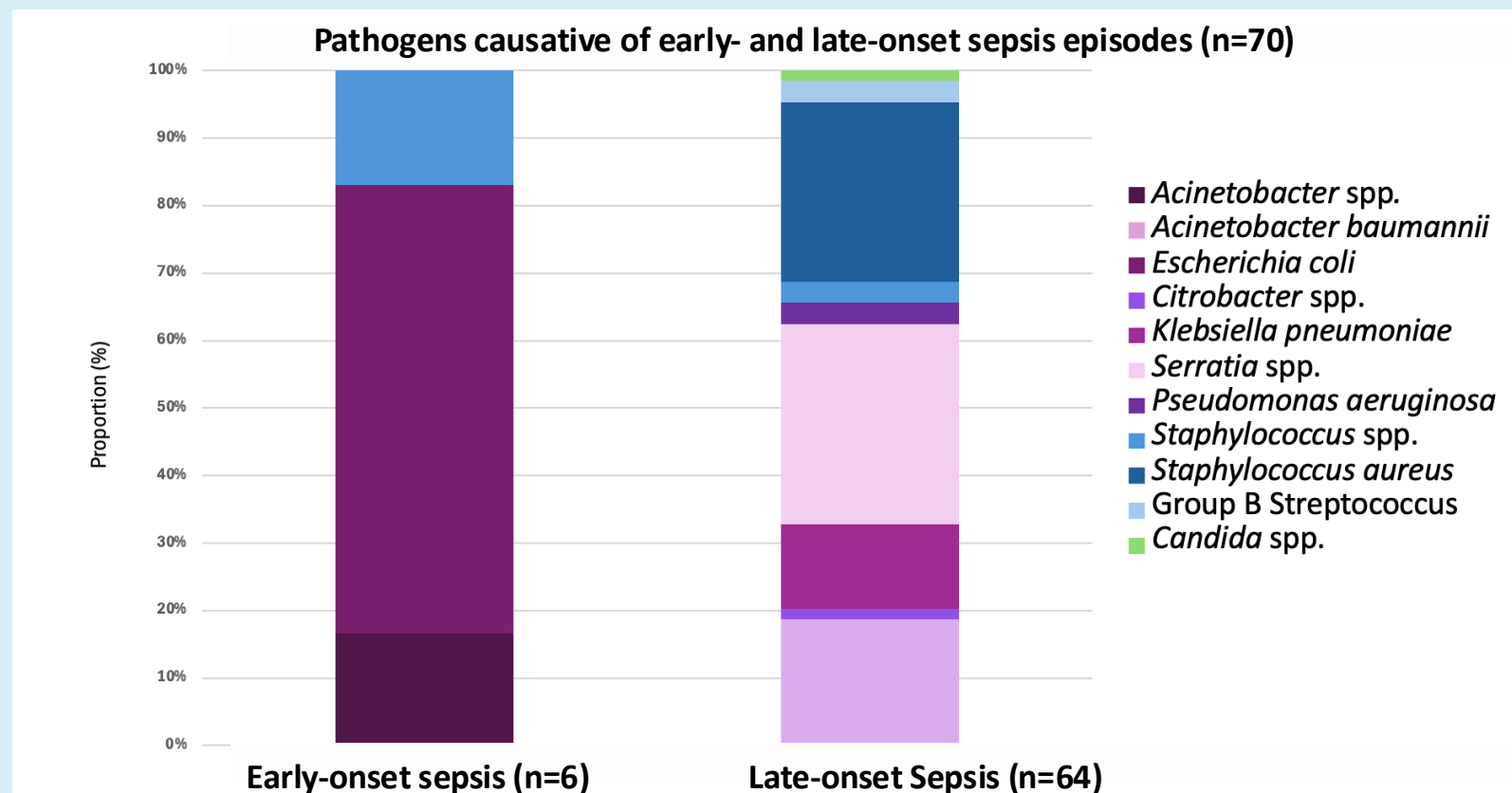


Figure 2. Pathogens causative of early- and late-onset sepsis episodes

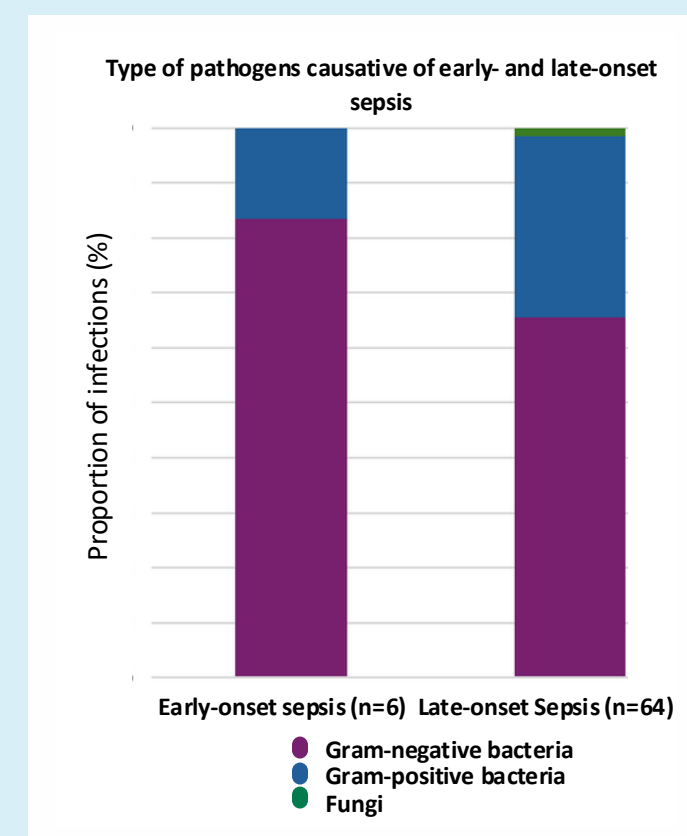


Figure 3. Pathogen types causative of early- and late-onset sepsis

Results:

Demographics:

- Enrolled **1046 neonates**
- Median gestational age: 34 weeks (Interquartile range (IQR): 31-36 weeks)
- Median birthweight: 1942g (IQR: 1456-2515g)
- Median length of NICU stay: 18 days (IQR: 10-34 days)
- 6% (60/1046) of neonates had an episode of culture-positive sepsis

Infection episodes:

- 1364 episodes of infection recorded**
- 997 (73%) early-onset community-acquired infections (infections acquired within the first 48 hours of life)
- 367 (27%) late-onset hospital-acquired infections (onset of clinical signs >48 hours after birth)
- 5% (68/1364) of infection episodes were culture-positive for a significant pathogen (Fig. 1).
- The most commonly-isolated gram-negative pathogens overall were **Serratia spp.** (n=19/70, 27%) **A. baumannii** (n=12/70, 17%) and **K. pneumoniae** (n=8/70, 11%) (Fig 2.)
- The majority of isolated pathogens in both early- and late-onset sepsis were gram-negative (Fig. 3).
- 40% (18/45) of tested gram-negative bacteria were resistant to carbapenems.**

Clinical outcomes at 28 days:

- Mortality rate overall of 14% (149/1046)
- 4% (38/1046) were alive but not back to baseline health
- 5% (53/1046) of enrolled were lost to follow-up and included in analysis as 'Alive'
- 12% (118/986) of neonates with culture-negative sepsis and 52% (31/60) of neonates with culture-positive sepsis died (Fig. 4).

28-day clinical outcomes for enrolled neonates (n=1046)

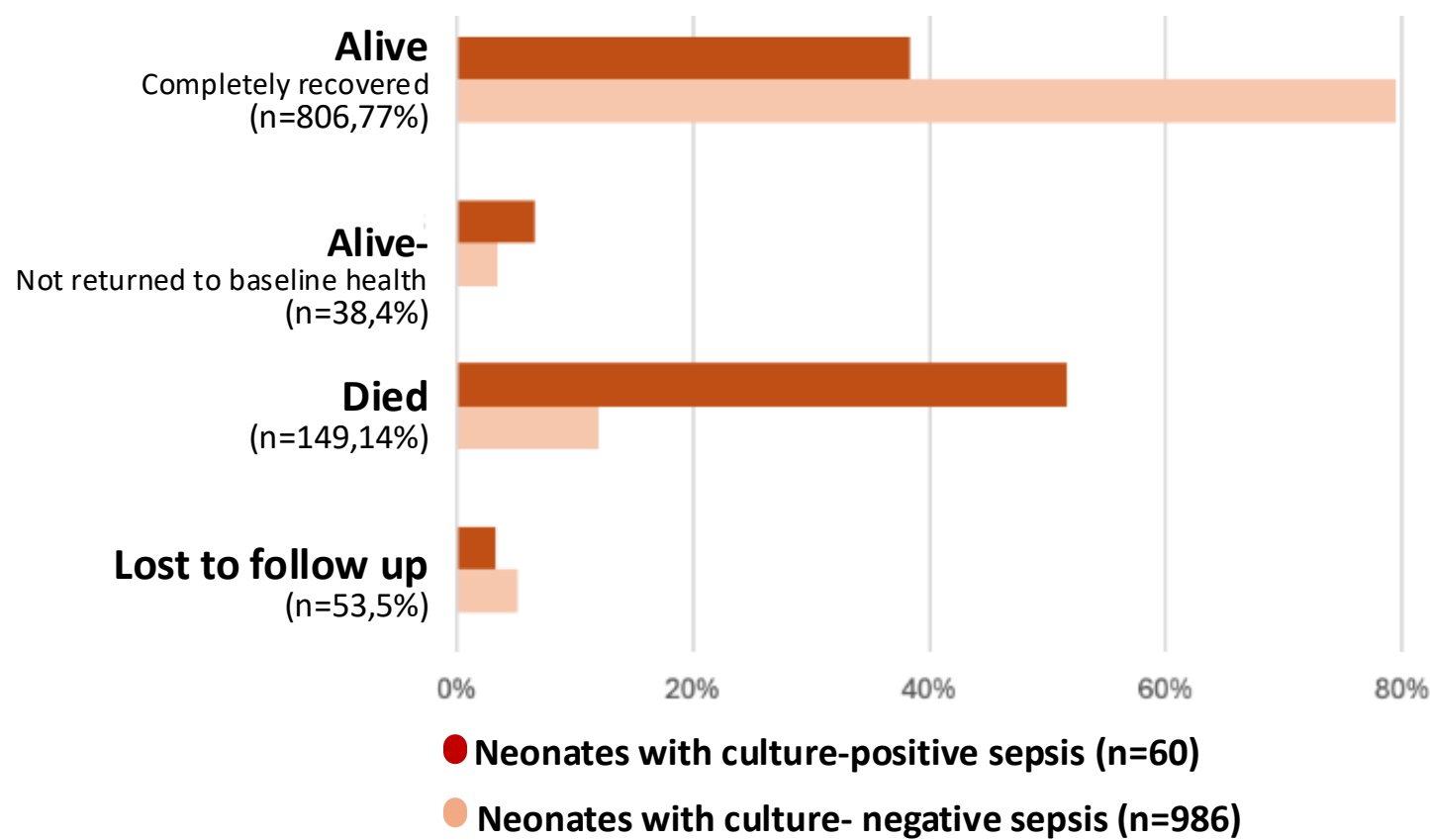


Figure 4. 28-day clinical outcomes for enrolled infants

Conclusion: There is a high burden of infection leading to high mortality rates in neonates at PGH. Gram-negative pathogens predominate and are associated with a high degree of resistance to empiric regimens for early- and late-onset sepsis. Culture-negative infections prevail, emphasising the need for empirical antibiotic guidelines that reflect geographic variability to ensure babies receive efficacious therapy.

References

- Williams P, Qazi S, Agarwal R, Velaphi S, Bielicki J, Nambiar S, et al. Antibiotics needed to treat multidrug-resistant infections in neonates. Bulletin of the World Health Organization 2022;100(12):797-807.
- Harrison M, Dickson B, Sharland M, Williams P. Beyond early- and late-onset neonatal sepsis definitions: What are the current causes of neonatal sepsis globally? A systematic review and meta-analysis of the evidence. Pediatric Infectious Disease Journal 2024
- Russell NJ, Barday M, Okomo U, Dramowski A, Sharland M, Bekker A. Early versus late onset sepsis in neonates - Time to shift the paradigm? Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases 2023.
- Clinically Oriented antimicrobial Resistance Network (ACORN). 2024 [cited 2024 June 7]. Available from: <https://acornmr.net/#/./README>

Acknowledgements: This project was funded by the National Health and Medical Research Council, Australia and the Sydney Infectious Disease Institute, University of Sydney