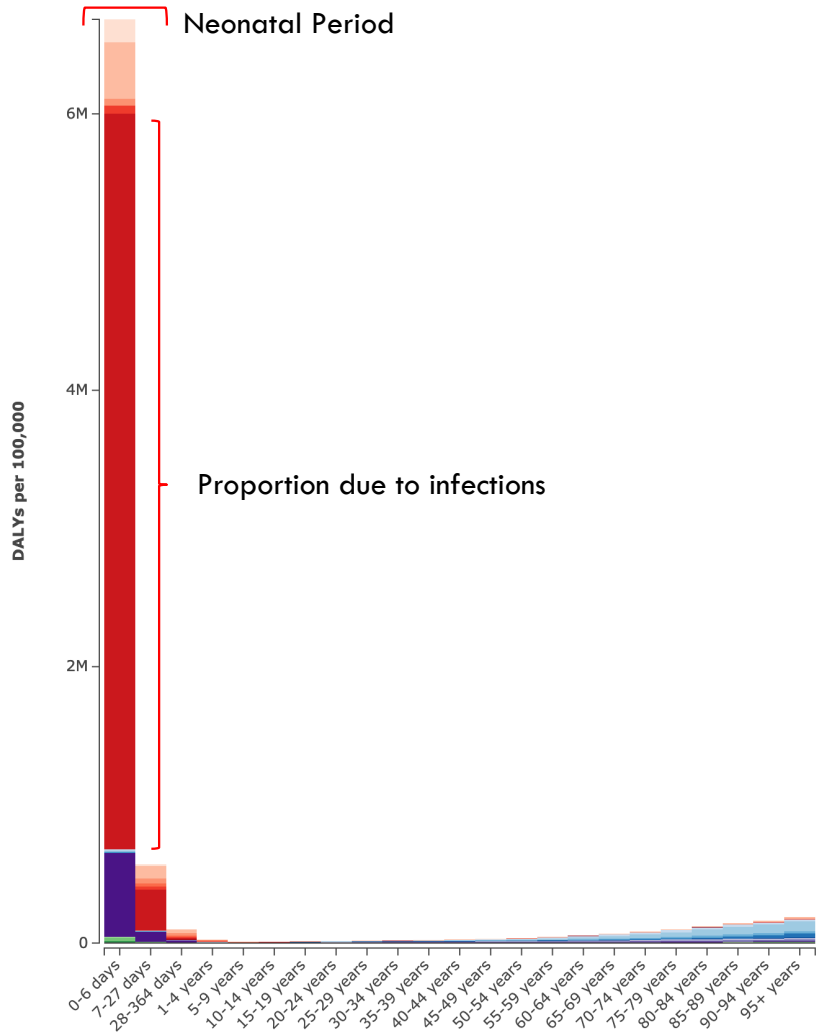
Gram-negative Neonatal Sepsis in the Asia Pacific

Asian Congress of Pediatric Infectious Diseases (ACPID)
August 2026

A/Prof Phoebe Williams
BSc BCom MBBS(Hons.) DCH MSc FRACP DPhil
Paediatrician & Infectious Diseases Physician
NHMRC Fellow, The University of Sydney

THE UNIVERSITY OF SYDNEY

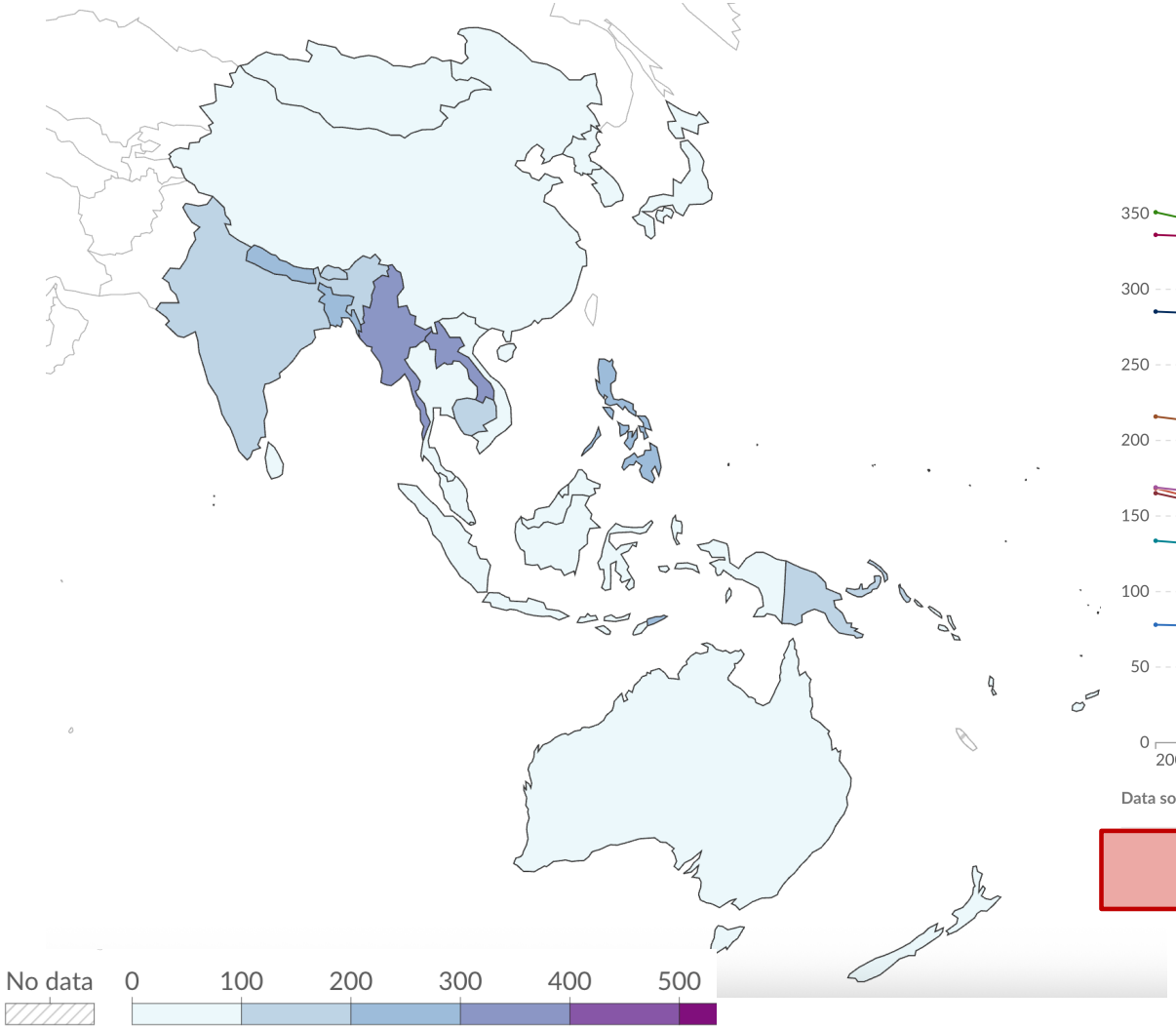
The first week of life continues to account for the greatest risk of death and disability – largely due to infections

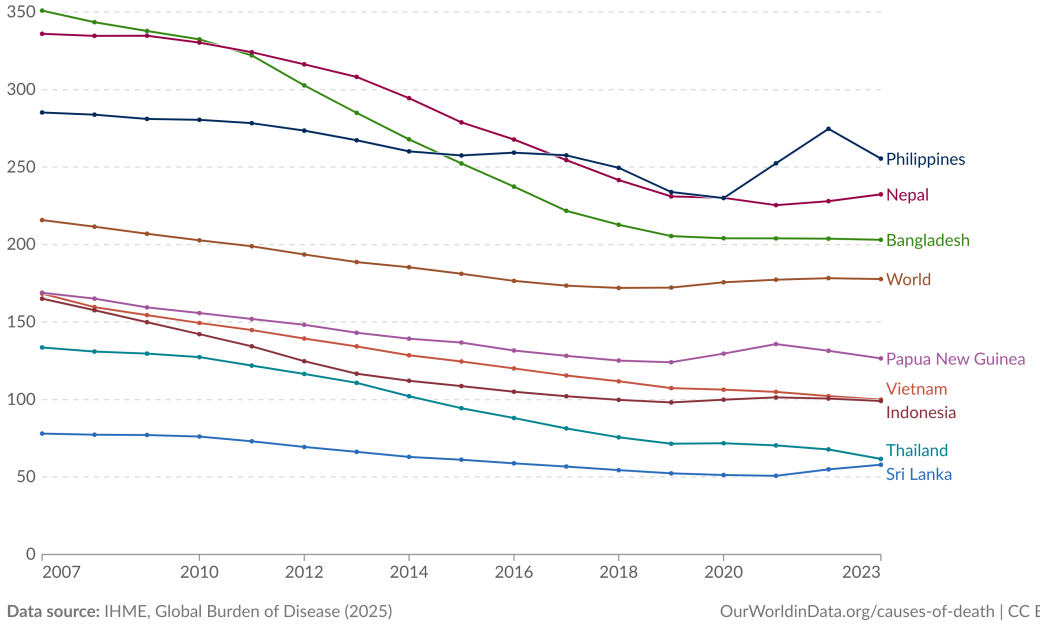


Institute for Health Metrics and Evaluation, 2019
https://vizhub.healthdata.org/gbd-compare/

Neonatal Sepsis Mortality across the Asia Pacific

Deaths per 100,000 infants





Stagnant progress in Neonatal Sepsis Mortality Rates Globally & Regionally

We have made minimal progress in diminishing neonatal sepsis, and AMR threatens to *increase* this morbidity & mortality burden

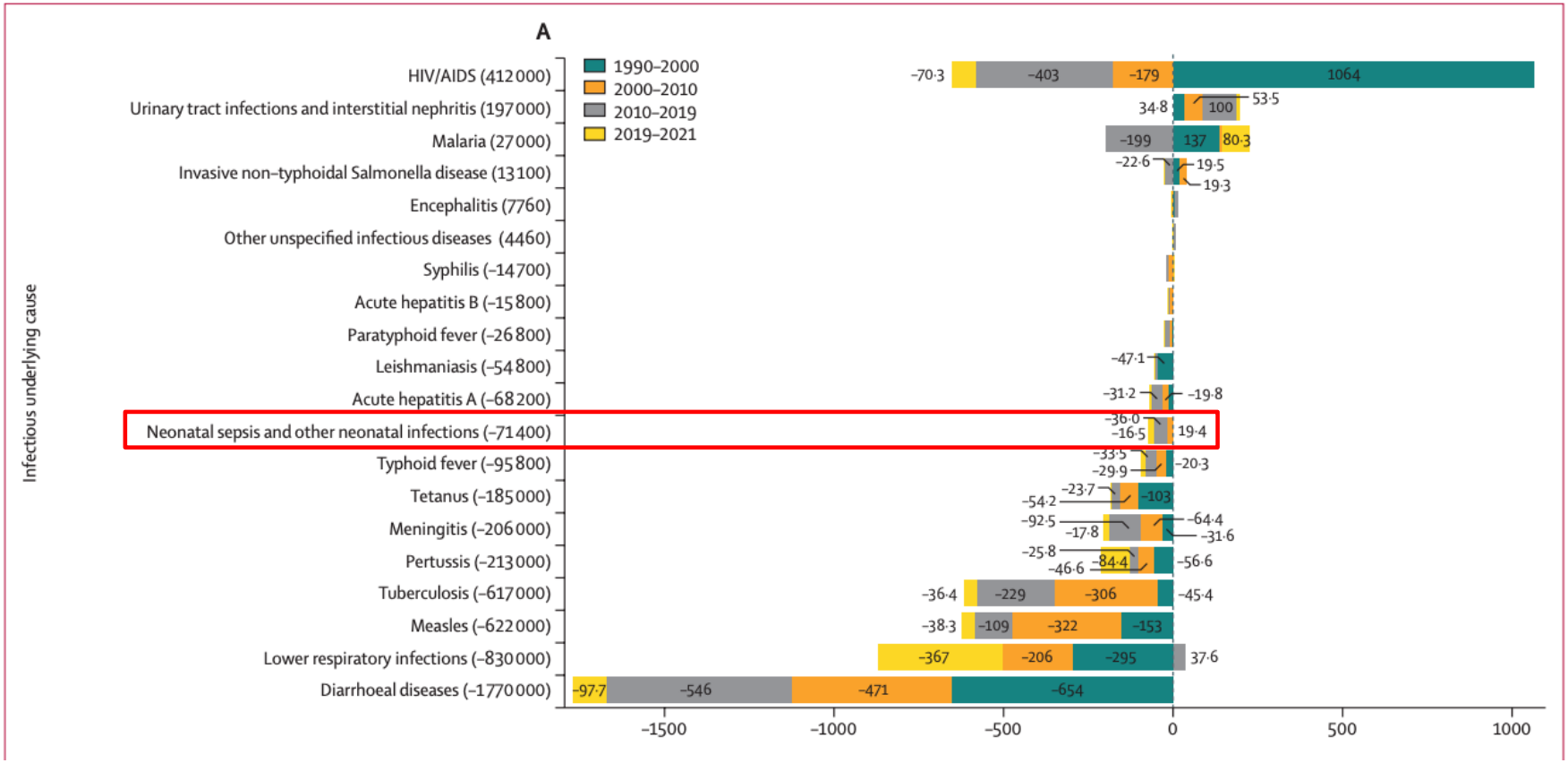
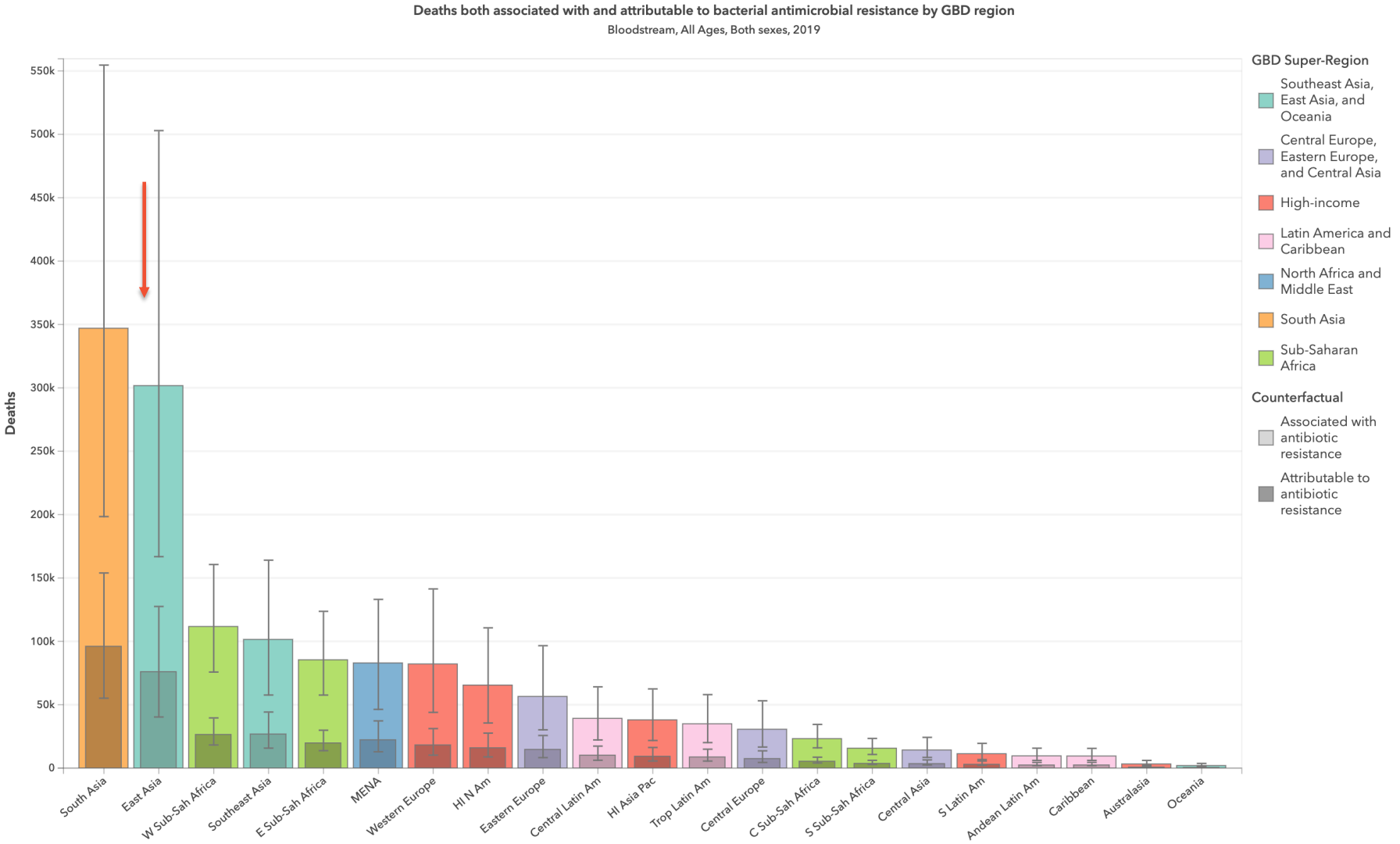


Figure 4: **Change in global sepsis-related deaths co-occurring with the leading 20 infectious (A) and non-infectious (B) underlying causes, by time period, from 1990–2021**
Each row represents the change in the number of sepsis-related deaths across a time period (1990–2000, 2000–2010, 2010–2019, and 2019–2021) for a given leading underlying cause (top 20 underlying causes for sepsis-related deaths in 1990), listed by change in mean deaths. The change in mean deaths is shown in parentheses. A bar to the right of 0 represents an increase in the number of cause-specific sepsis deaths and a bar to the left of 0 represents a decrease in the number of cause-specific sepsis deaths. For readability, values less than 15 000 in panel A and values less than 1000 in panel B are not displayed.

GBD 2021 Collaborators. Lancet Global Health, 2025.

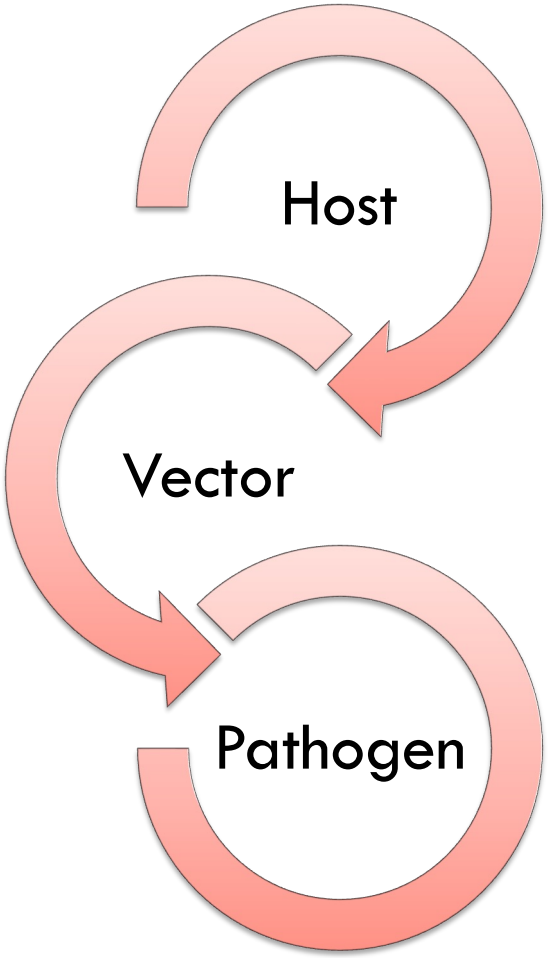
The greatest threat to neonates is rapidly rising AMR, concentrated in Asia



The l

Murray CJL et al.
Lancet 2022;399:629e55

Why are neonates so at risk of infection?



1. Vulnerable host (esp. preterm):

- Immunologically immature: Decreased polymorphonuclear leucocyte and cell-mediate immune function
- Less diverse microbiome: Particularly following exposure to intrapartum antibiotics

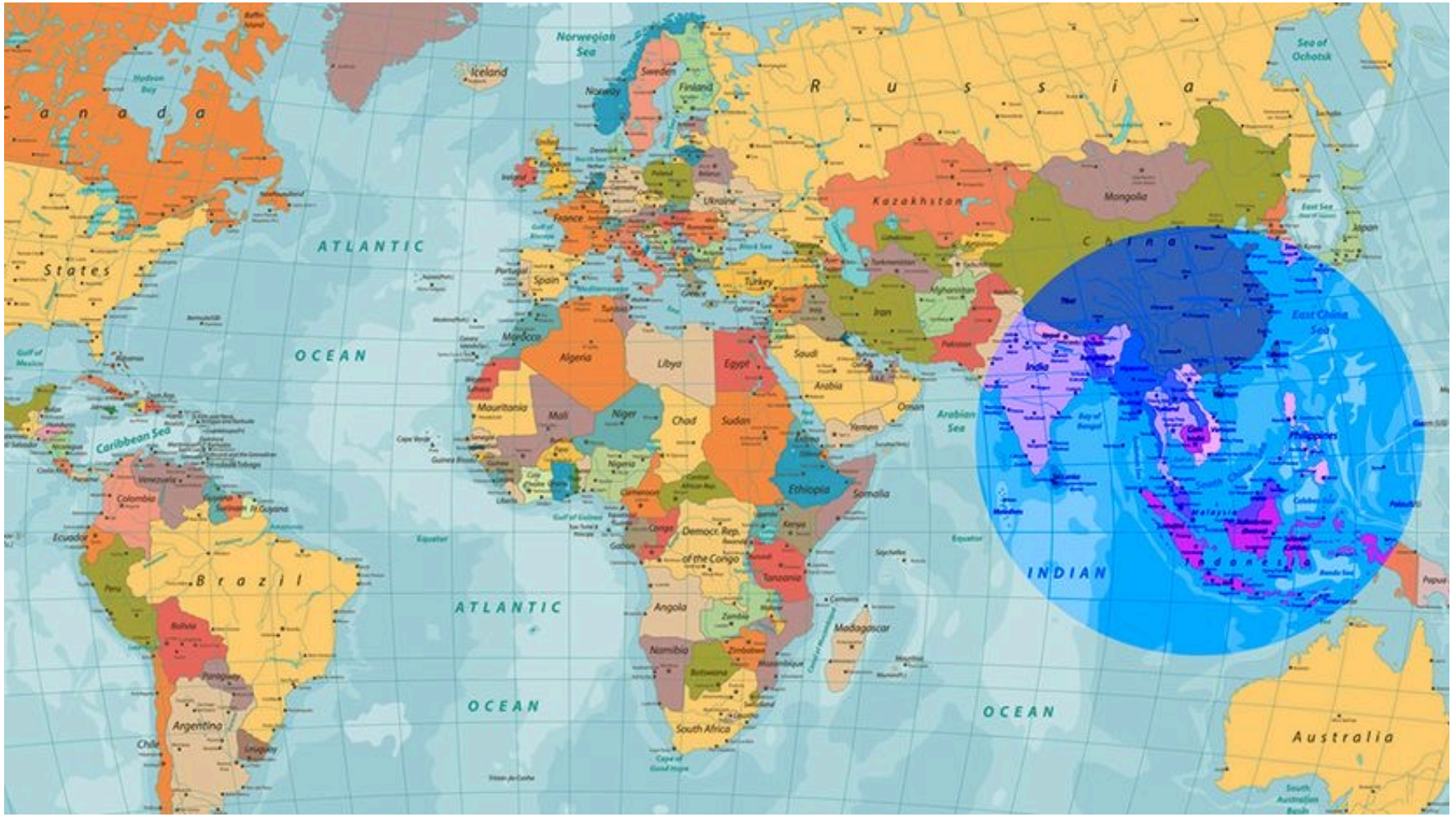
2. Risk of hospital-acquired infections

- Multiple invasive procedures: ventilation, long line access
- Prolonged hospitalisation → risk of exposure to multiple empirical courses of antibiotics, enhancing selective pressure → risk of MDR infections
- Exposure to multiple caregivers: parents, carers, healthcare workers (colonisation risk)

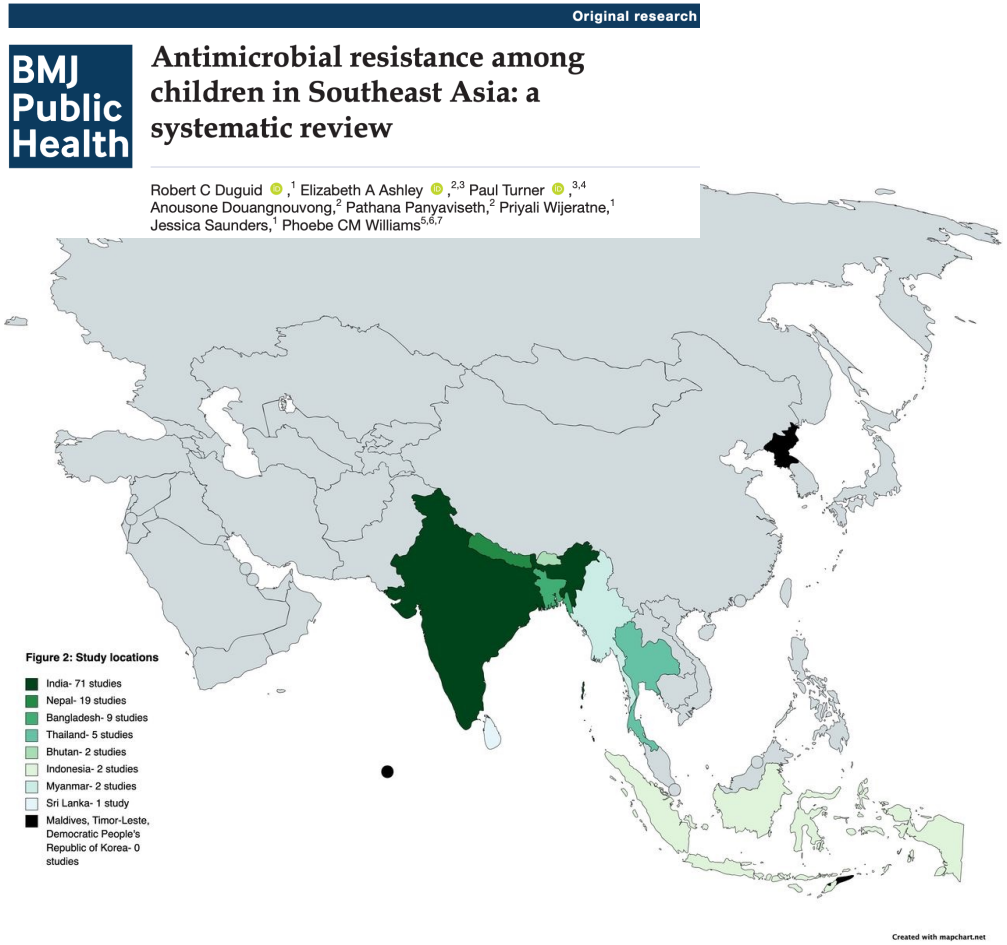
3. Rapidly rising gram-negative bacteria burden

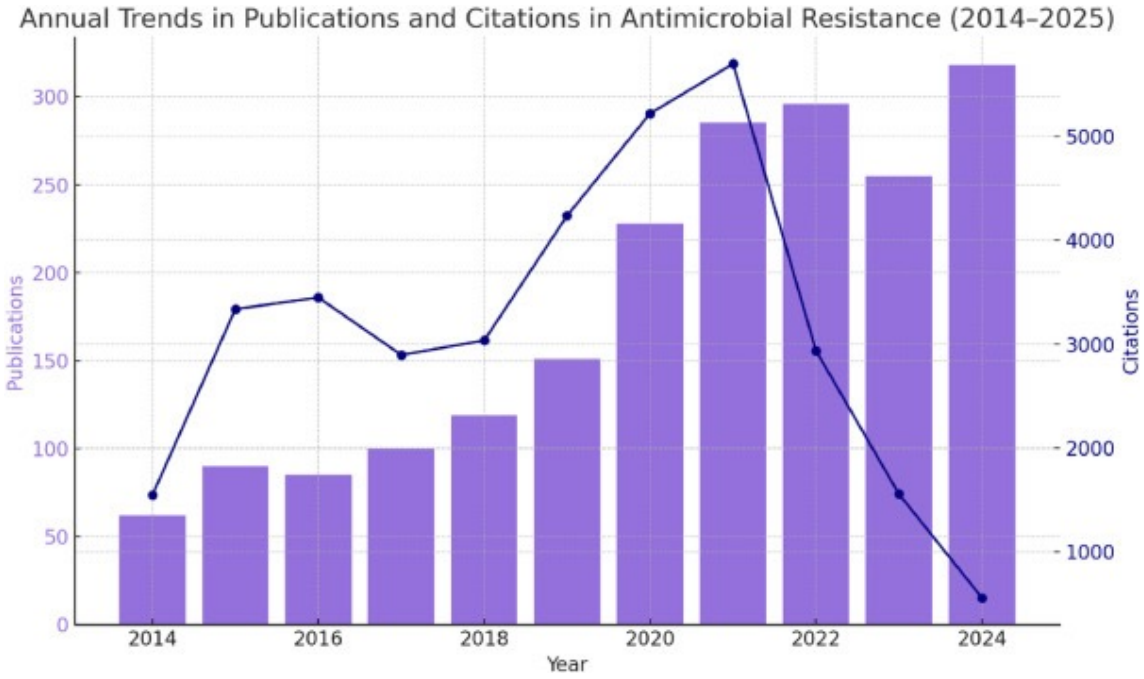
- Plasmid-mediated resistance → spread of MDR infections
- Dry antibiotic pipeline to treat MDR infections, particularly for neonates

This small circle contains over half the world's population



Despite the Asia Pacific Bearing the Greatest Burden of AMR, published data from the region are scarce





Borromeo *et al. 2025*
Southeast-Asian landscape of antimicrobial resistance research

The need for surveillance data

'Without data, we can't prove anything about the clinical burden we see – we need more data from Indonesia. Data can make things happen."

THE UNIVERSITY OF SYDNEY

Prof. Dr. dr. Sri Rezeki Hadinegoro, Sp.A.(K).

Fakultas Kedokteran

What is the burden of AMR in neonatal sepsis across the Asia Pacific? Findings from the NeoSEAP study

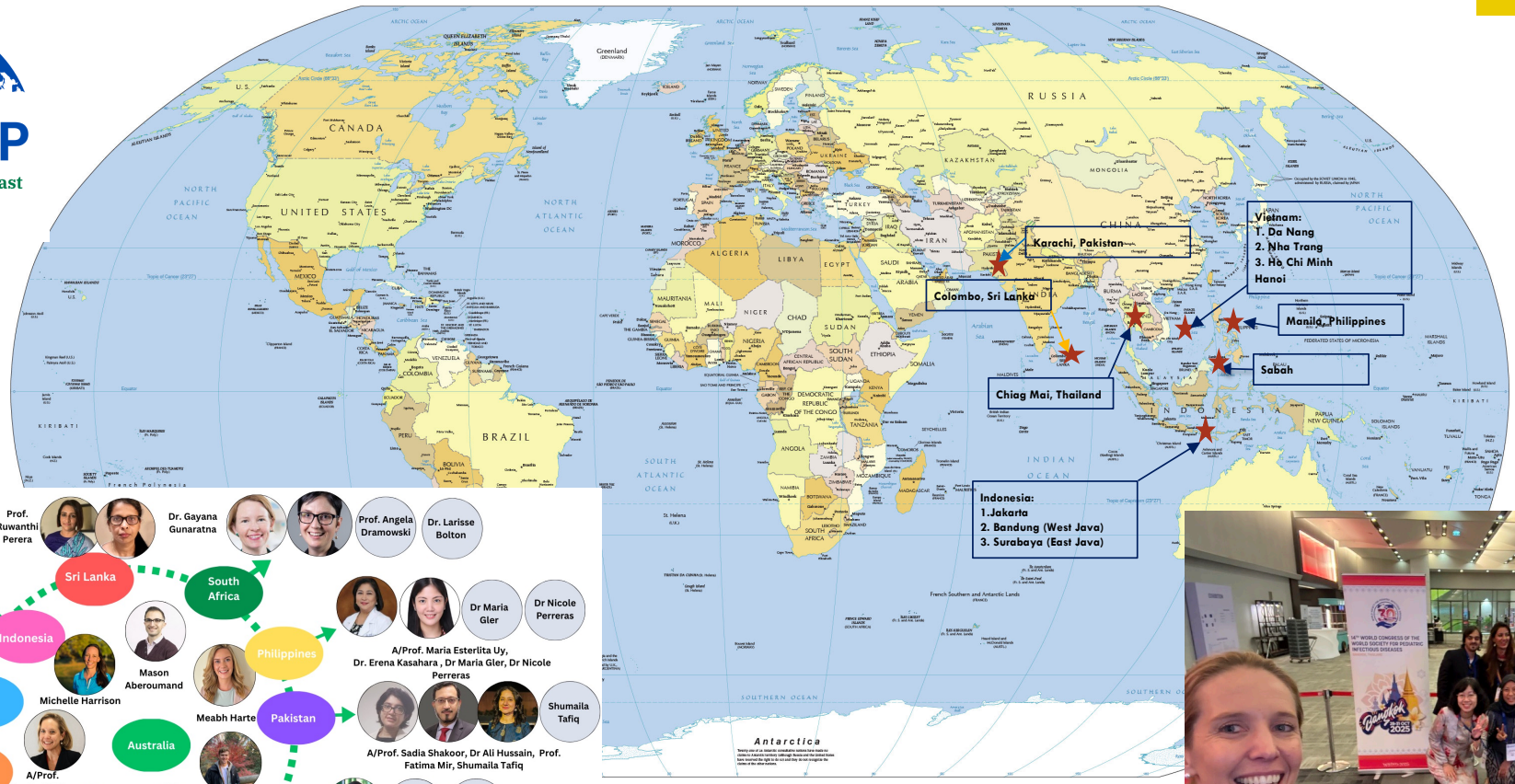
Neonatal Sepsis in South East Asia and the Pacific

Australian Government
National Health and Medical Research Council

NHMRC

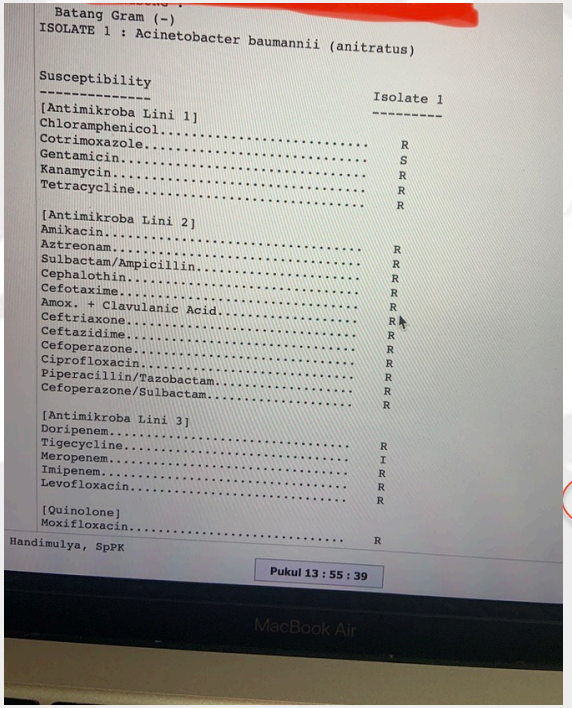
Gates Foundation

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific



Dr. Nina Dwi Putri, Dr. Leny Kartina and Dr. Riyadi Adrizain

Indonesia


Batang Gram (-)
ISOLATE 1 : Acinetobacter baumannii (anitratus)
Susceptibility
Isolate 1
[Antimikroba Lini 1]
Chloramphenicol R
Cotrimoxazole S
Gentamicin R
Kanamycin R
Tetracycline R
[Antimikroba Lini 2]
Amikacin R
Aztreonam R
Sulbactam/Ampicillin R
Cephalothin R
Cefotaxime R
Amox. + Clavulanic Acid R
Ceftriaxone R
Ceftazidime R
Cefoperazone R
Ciprofloxacin R
Piperacillin/Tazobactam R
Cefoperazone/Sulbactam R
[Antimikroba Lini 3]
Doripenem R
Tigecycline I
Meropenem R
Imipenem R
Levofloxacin R
[Quinolone]
Moxifloxacin R
Handimulya, SpPK
Pukul 13 : 55 : 39
MacBook Air

The Philippines

- Population 110m
- ~1.7m births per year

- **Philippine General Hospital:** 5,000 admissions to NICU each year

- Neonatal sepsis case fatality rate
  - → 30% in 2010
  - → 70% in 2020
  - -Largely due to MDR *Acinetobacter baumannii* and *Klebsiella* spp. outbreaks

What is the likelihood the currently-recommended empirical regimens are efficacious in treating neonatal sepsis?

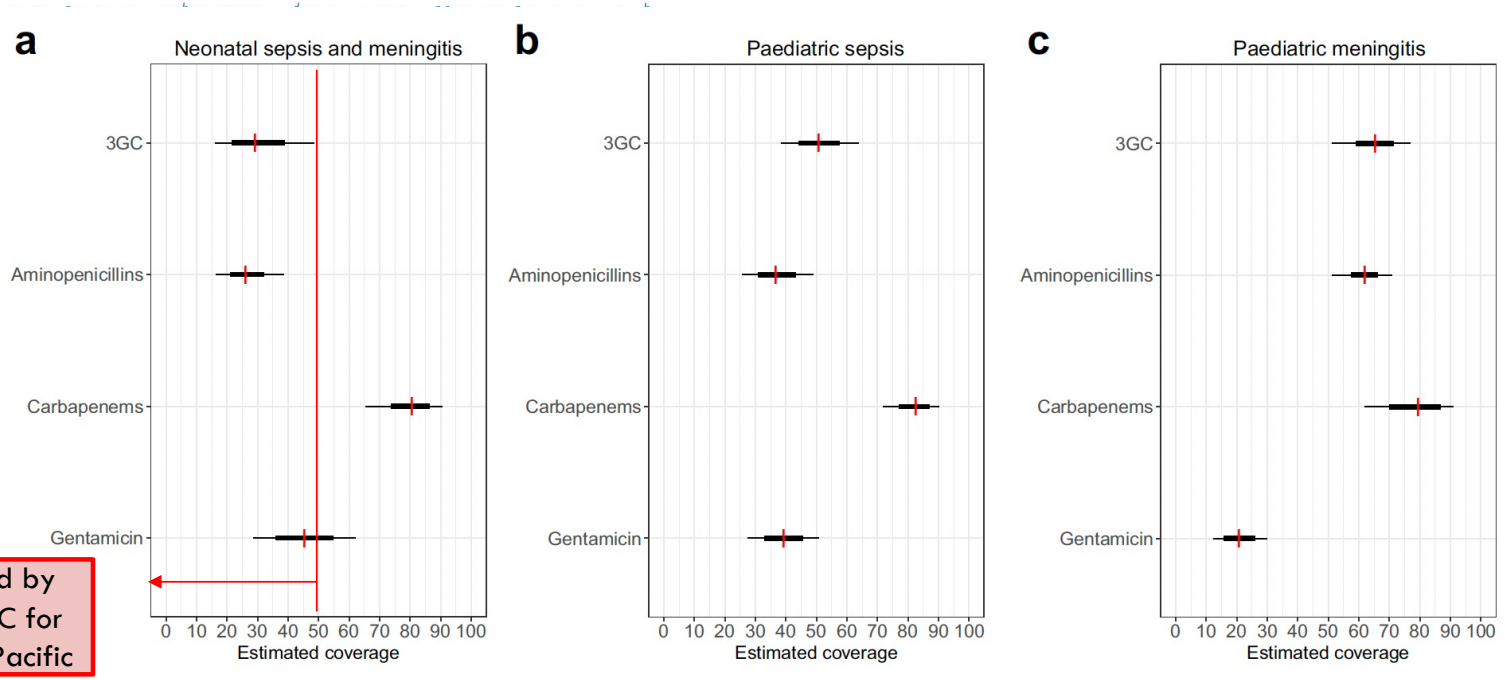
Findings from the NeoSEAP study, 2024

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific

Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific

Phoebe C. M. Williams,[a,b,c,*] Mark Jones,[a] Th
Priyali Wijeratne,[b] Anousone Douangnouvon

[a]Faculty of Medicine, School of Public H
[b]Department of Infectious Diseases, Sydr
[c]Sydney Institute of Infectious Diseases (
[d]Department of Infectious Diseases, Roy
[e]Department of Global Health, London S
[f]Lao-Oxford Wellcome Trust Research Ur
[g]Centre for Tropical Medicine and Globa
[h]Cambodia Oxford Medical Research Uni



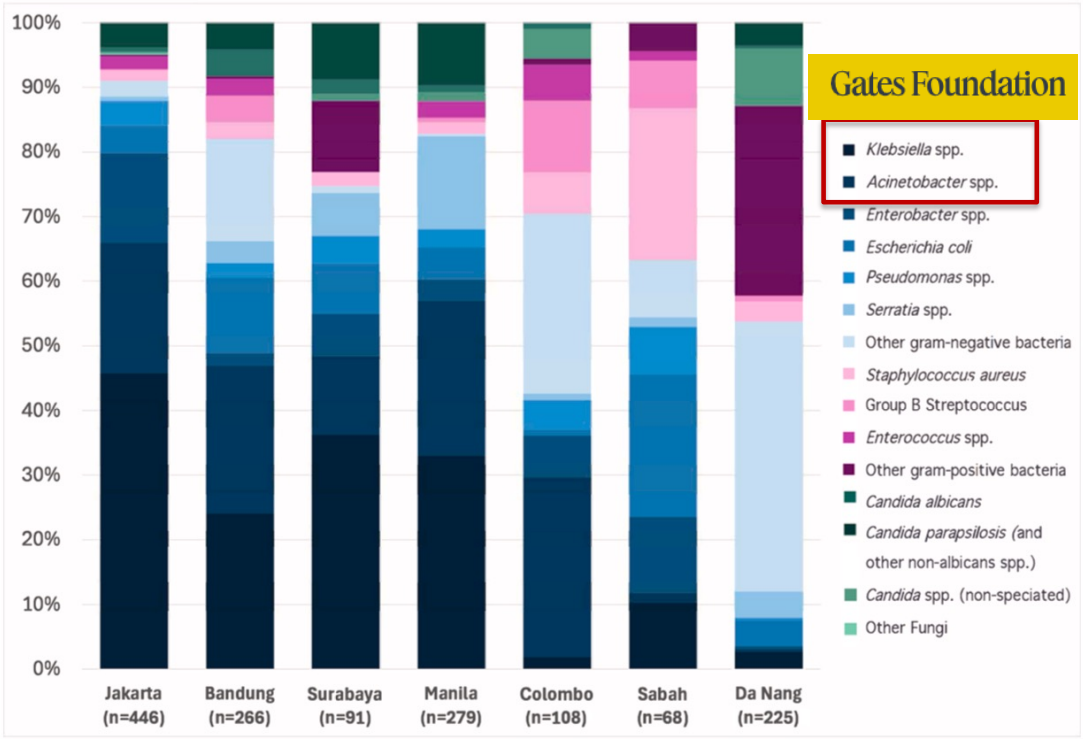
<50% coverage provided by ampicillin/gentamicin/3GC for neonates in SE Asia & the Pacific

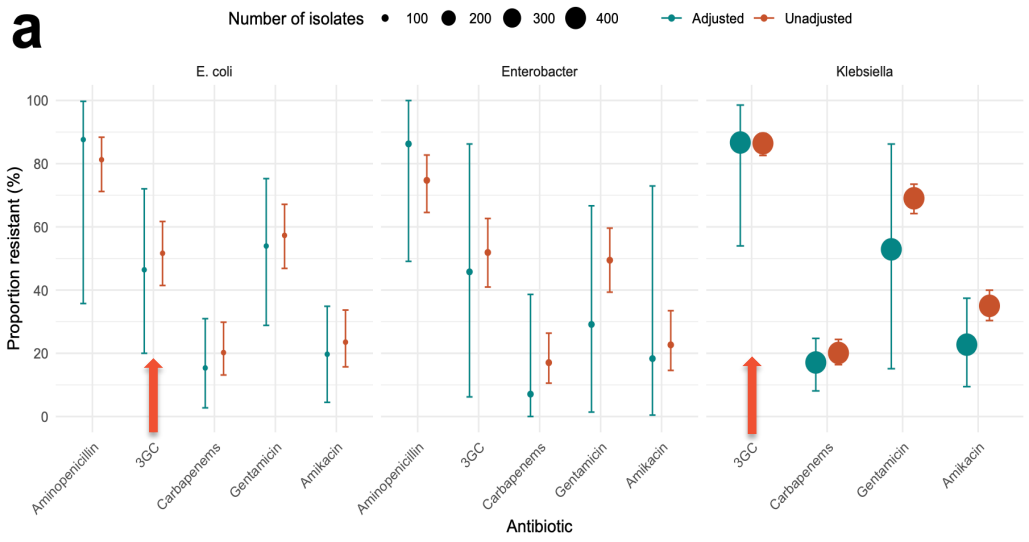
Fig. 2: Coverage estimates by syndrome and antibiotic. Note: 3GC = Third-generation cephalosporins (ceftriaxone, cefotaxime); aminopenicillin incorporates ampicillin and amoxicillin non-susceptibility data, and carbapenem incorporates published non-susceptibility data for both meropenem and imipenem. The thin and thick lines correspond to the 80% and 50% credible intervals.

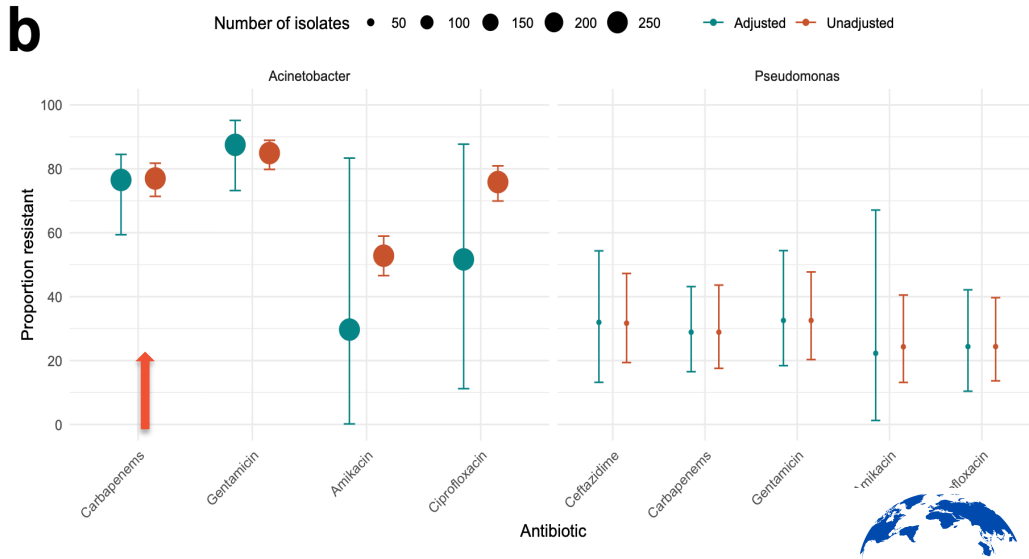
Pathogen distribution and antimicrobial resistance among neonatal bloodstream infections in Southeast Asia: results from NeoSEAP, a multicentre retrospective study

Benjamin F. R. Dickson,[a,b] Michelle Harrison,[a,b] Maria Esterlita T. Villanueva-Uy,[c,d] Nina Dwi Putri,[e,f] Riyadi Adrizain,[g,h] Leny Kartina,[i,j] Gayana P. S. Gunaratna,[k,l] Hoang T. Tran,[m,v] Nguyen X. Huong,[o] Siew M. Fong,[p] Erena S. Kasahara,[d] Distyayu Sukarja,[e] Tetty Yuniati,[g,h] Martono Utomo,[i,j] Nambage S. Chandrasiri,[f] Chau H. M. Le,[m,n] Nguyen T. K. Trinh,[o] Ng Boon Hong,[p] Hoang N. T. Thuy,[q] Tran T. C. Tu,[r] Le T. Hong,[s] Jannah Baker,[a] Mark Jones,[a] Thomas L. Snelling,[a] Mike Sharland,[t] and Phoebe C. M. Williams,[a,b,u,*] on behalf of the NeoSEAP Consortium

Analysis of 14,804 blood cultures collected over 2019-2020; of which 2,131 were positive (1,483 with significant pathogens)







NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific

Fig. 3: **Distribution of culture-positive pathogens isolated across all sites (n = 1483).** Pink = gram-positive bacteria, blue = gram-negative bacteria, green = fungi.

Coverage gaps in empiric antibiotic regimens used to treat serious bacterial infections in neonates and children in Southeast Asia and the Pacific

Phoebe C. M. Williams,[a,b,c,*] Mark Jones,[a] Thomas L. Snelling,[a] Robert Duguid,[b] Nerida Moore,[d] Benjamin Dickson,[a,e] Yue Wu,[a] Jessica Saunders,[b] Priyali Wijeratne,[b] Anousone Douangnouvong,[f] Elizabeth A. Ashley,[f,g] and Paul Turner[a,h]

nature communications

Article https://doi.org/10.1038/s41467-026-74261-z

Diagnostic challenges and Gram-negative pathogen dominance in early- and late-onset neonatal infection in Manila, Philippines

Received: 2 March 2026

Michelle L. Harrison[1,2], Maria E. Villanueva-Uy[3,4], Erena Kasahara[3,4], Julie Jaynney Caparas[4], Nover Edward Duarte[4], Alkim Ozaygen[1], Patrick Cahill[1],

MATERNAL-NEONATAL REPORTS

OPEN

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

Michelle L. Harrison, MPH,† Benjamin F.R. Dickson, MPH,*† Mike Sharland, FRCPCH,‡ and Phoebe C.M. Williams, DPhil*†§¶*

NEOSEAP

Neonatal Sepsis in Southeast Asia and The Pacific

OPEN

CURRENT OPINION

The challenge of antimicrobial resistance in the Asia-Pacific: a pediatric perspective

Nguyen Xuan Huong[a], Michelle Harrison[b], Erena Kasahara[c], Ben Marais[b], Nina Dwi Putri[d] and Phoebe CM Williams[e,f,g]

Original research

BMJ Public Health

Antimicrobial resistance among children in Southeast Asia: a systematic review

Robert C Duguid,[1] Elizabeth A Ashley,[2,3] Paul Turner,[3,4] Anousone Douangnouvong,[2] Pathana Panyaviseth,[2] Priyali Wijeratne,[1] Jessica Saunders,[1] Phoebe CM Williams[5,6,7]

Original research

BMJ Global Health

Epidemiology of sepsis in hospitalised neonates in Indonesia: high burden of multidrug-resistant infections reveals poor coverage provided by recommended antibiotic regimens

Nina Dwi Putri,[1] Benjamin FR Dickson,[2,3] Riyadi Adrizain,[4] Leny Kartina,[5] Jannah Baker,[2] Distiayu Sukarja,[1] Fabiola Cathleen,[1] Dominicus Husada,[6] Martono T Utomo,[7] Tetty Yuniati,[8] Adhi K Suginali,[8] Michelle Harrison,[2,3] Michael Sharland,[9] Phoebe CM Williams[2,3,10]

Nature Communications https://doi.org/10.1038/s41467-026-75634-0

Article in Press

Delineating the risk factors, sources of acquisition and clinical outcomes in neonates colonised with multidrug-resistant bacteria: the NeoCol study

Received: 18 January 2026
Accepted: 15 June 2026
Published online: 20 July 2026
Cite this article as: Putri, N.D., Harrison, J., Dickson, B.F. *et al.*

Nina Dwi Putri, Jackson Harrison, Benjamin F. R. Dickson, Delly Chipta Lestari, Jessica Ramsay, Michelle Harrison, Wisnu Tafroji, Rima Irwinda, Adhi Teguh Perma Iskandar, Amanda Rumondang, Aqila Sakina Zhafira, Margaretha Sirenna Valeria, Mona Mostaghim, Annaleise R. Howard-Jones, Paul Turner, Clara Grazian & Phoebe C. M. Williams

ORIGINAL ARTICLE OPEN ACCESS

Antimicrobial Resistance and Infant Mortality in Sri Lanka: A Retrospective Cohort Study

Gayana P. S. Gunaratna[1,2] | Michelle L. Harrison[3,4] | Benjamin F. R. Dickson[3,4] | Rajeev Sathanandaraja[1] | T. M. Ruwanthi Perera[1,5] | Nambage Shirani Chandrasiri[1] | Anasuya Sutharson[1] | Jannah Baker[3] | Phoebe C. M. Williams[3,4,6]

NeoSEAP: Aims and Findings

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific

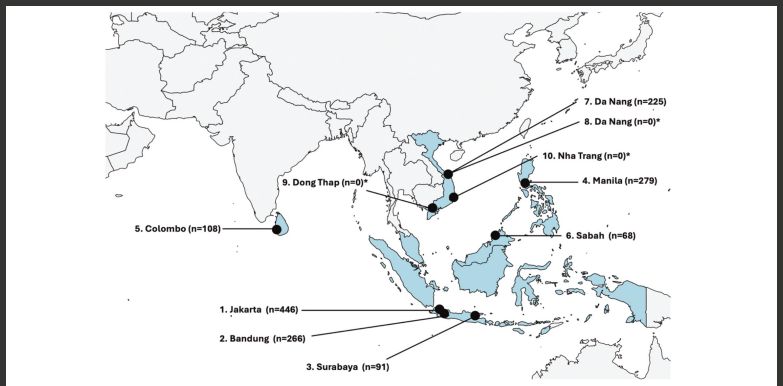
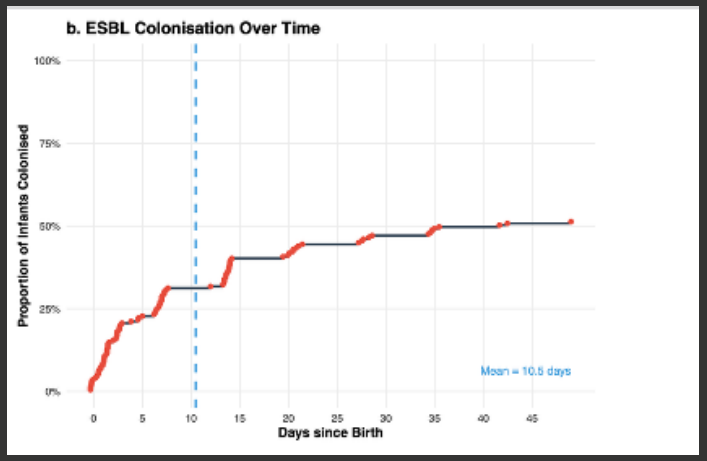


Fig. 1: **Map of included countries and study sites.** The number preceding each city denotes site number. The number in parentheses denotes number of positive blood cultures at each site for the period of 2019–2020 inclusive. *Private hospital.

www.thelancet.com Vol 62 September, 2025

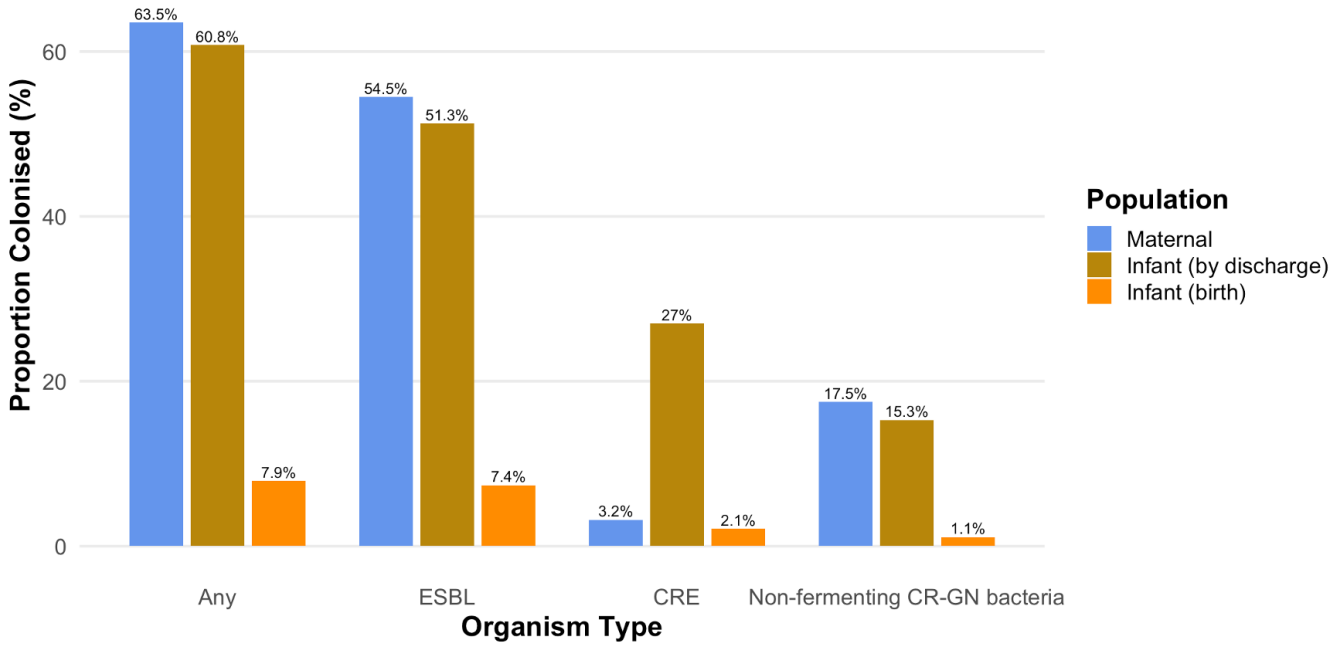


Identify the epidemiology of neonatal sepsis, the burden of AMR and advocate for access to antibiotics to treat these infections

Identify how, when and why babies are colonised with, then infected by, MDR gram-negative pathogens

How and when are babies colonised with MDR pathogens?

Findings from the NeoCol Jakarta Study



ESBL colonisation is common in mothers at delivery, yet CRE colonisation is rare

Neonates admitted to the NICU quickly become colonised with CREs, with 1 in 4 positive by discharge

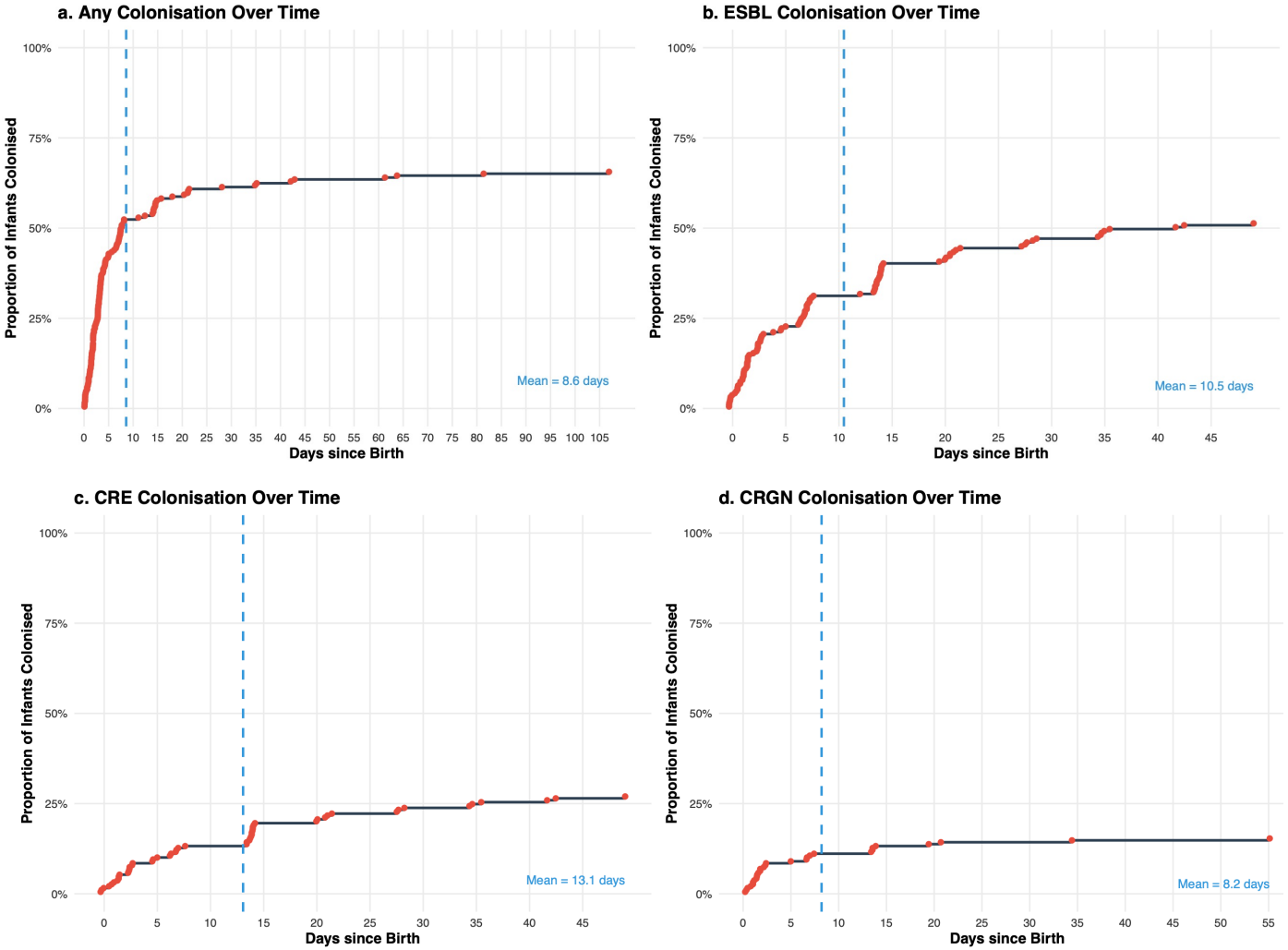
Figure 1 *Overall proportion of maternal and infant colonisation with gram-negative bacteria, by resistance mechanism type.*

Note: ESBL = extended-spectrum beta-lactamase producing; CRE = carbapenem-resistant Enterobacterales; CR-GN = carbapenem-resistant non-fermenting bacteria (*Acinetobacter* spp., *Pseudomonas* spp.)

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific

How and when are babies colonised with MDR pathogens?



Kaplan–Meier curves summarising the cumulative time to neonatal colonisation of 189 hospitalised neonates, with:

a. any resistant gram-negative bacteria

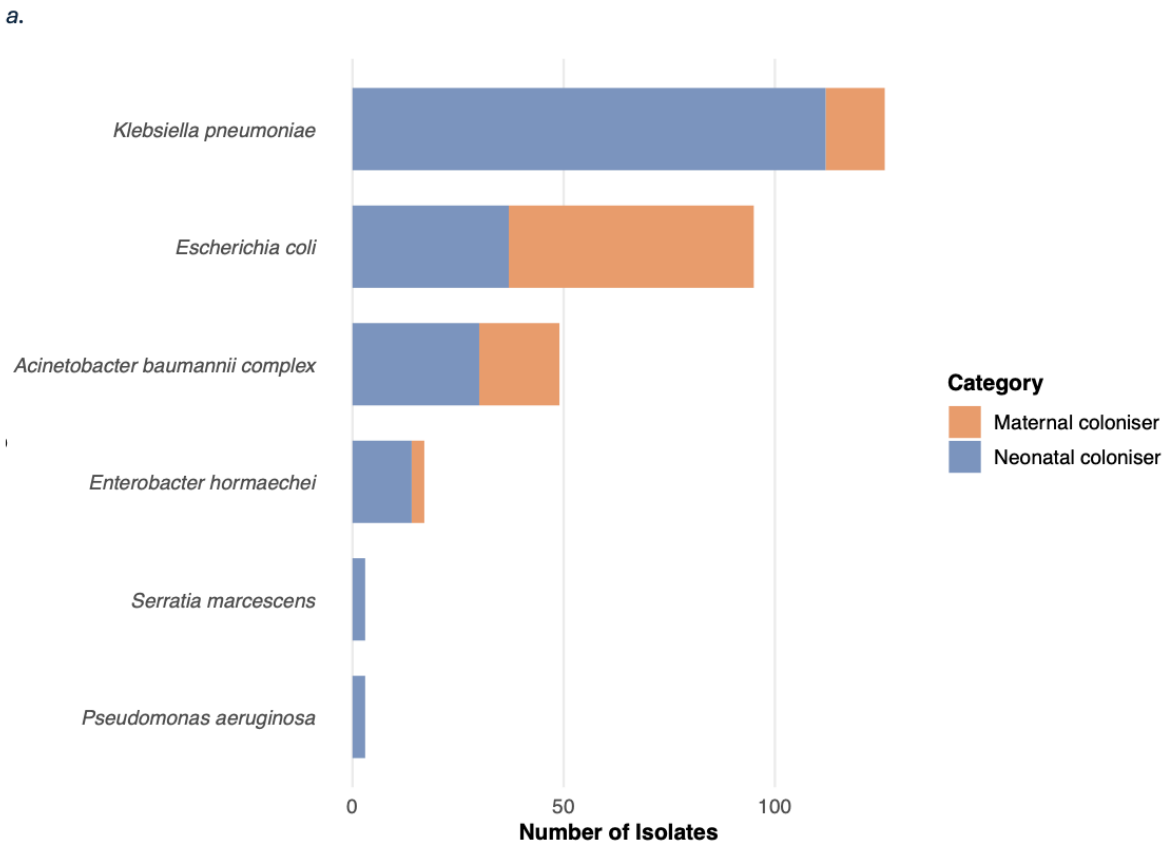
b. ESBL-producing bacteria

c. carbapenem-resistant Enterobacterales

d. carbapenem-resistant gram-negative (non-fermenting) bacteria (including *Acinetobacter* spp. and *Pseudomonas* spp.)

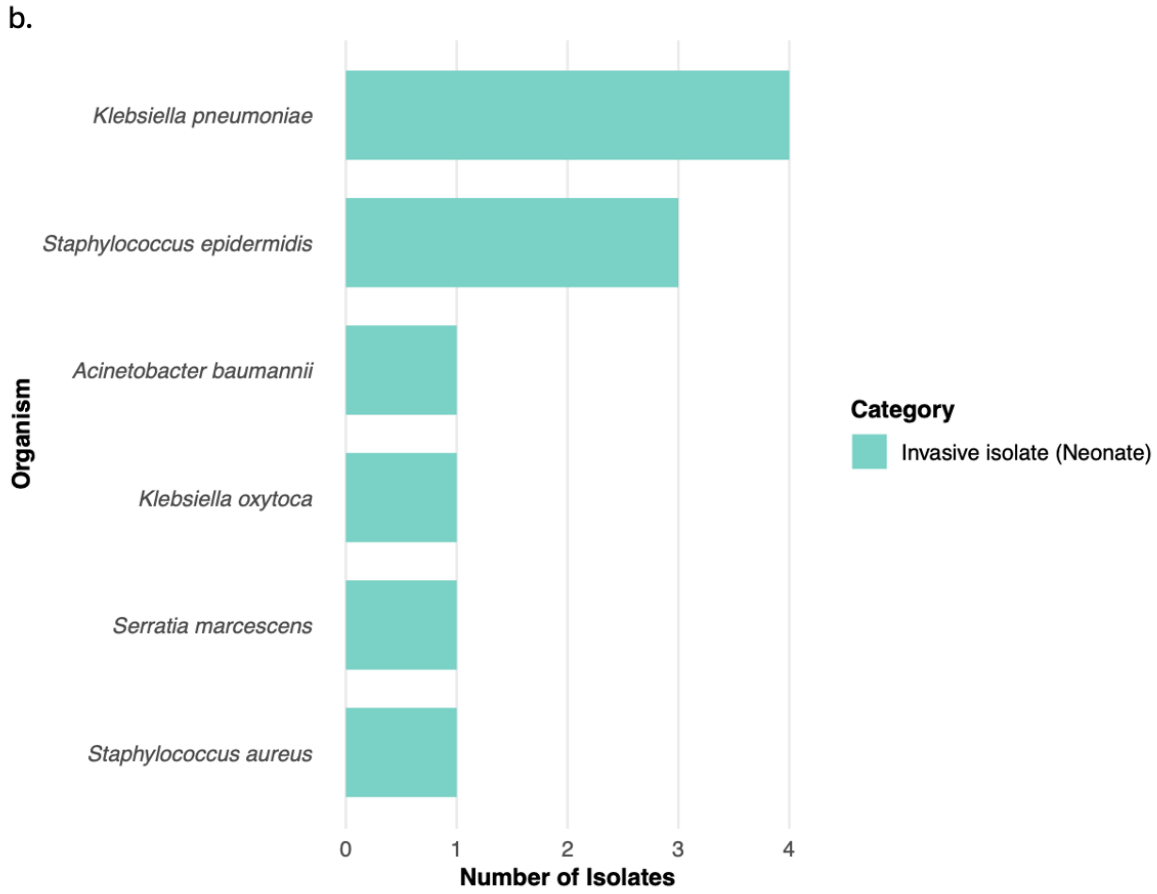
What bacteria are most frequently colonising Mothers & Babies?

Findings from the NeoCol Jakarta Study



What bacteria are most frequently causative of culture-positive neonatal sepsis?

Findings from the NeoCol Jakarta study



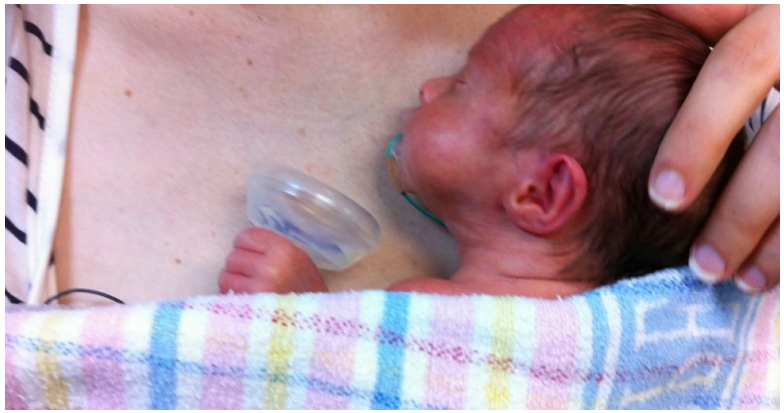
Key Findings from the NeoCol Jakarta Study:

Risk factors and clinical outcomes

- Neonates colonised with MDR bacteria were more likely to:
  - Have been exposed to **antibiotics** prior to colonisation (63%, vs 24%, p<0.001)
  - Require a **longer hospital stay** (16 days vs 2 days, p<0.001)
  - Experience episodes of **sepsis** (including culture-negative) following colonisation (62% vs 24%, p<0.001).

- Infection episodes (culture-negative & culture-positive) occurred in **almost half of all infants** (47%, 89/189)
  - 19 of these infants (10%) experienced >1 infection episode during their hospital admission

- Most culture-positive neonatal infections (91%, 10/11) were **not** caused by previously identified colonising bacteria.



MDR neonatal infections are not just an issue for resource-constrained healthcare settings

... cultures by phone.

Bottle Type	Paediatric	
Result	POSITIVE	After <24 hours incubation
GRAM STAIN		
Gram Stain	Gram negative bacilli	*
Detected In	Paediatric bottle	
Report to follow		
ISOLATES		
Growth of...	Enterobacter cloacae complex (First isolate) from paediatric bottle	
Growth of...	Enterobacter cloacae complex (Second isolate) from paediatric bottle	

SENSITIVITIES:

	Enterobacter cloacae complex (First isolate)	Enterobacter cloacae complex (Second isolate)
Amoxycillin + clavulanate	Resistant	Resistant
Ampicillin	Resistant	Resistant
Aztreonam	Resistant	
Cefepime	Resistant	Susceptible
Cefotaxime	Resistant	Resistant
Ertapenem	Resistant	
Gentamicin	Susceptible	Susceptible
Meropenem	Resistant	Susceptible
Piperacillin + tazobactam	Resistant	Resistant
Tobramycin	Susceptible	Susceptible

Comments:
BC Coliform sens (Org1) Comments:
This isolate is a Carbapenem Resistant Enterobacterales (CRE).

Successful Use of Cefiderocol to Treat a Multidrug-resistant *Stenotrophomonas maltophilia* Ventilator-associated Pneumonia in an Extremely Preterm Neonate

Archana Koirala, MBChB, MIPH,†‡§ Bharath Krishnappa, MBBS, MD,¶ Caroline Banh, BSc Adv, MBBS, MIPH,*‖ Ulrike Brandenburg, MD,¶ Michael Findlay, BMedSc, MBBS,*‖ and Phoebe C. M. Williams, MBBS(Hons), MSc(Global Health), DPhil†‡§***

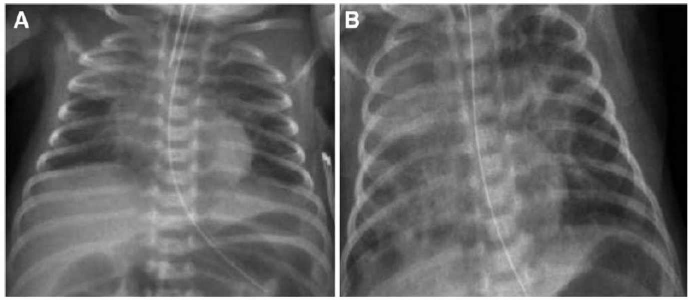


FIGURE 1. Chest radiograph of the 24+6 gestational age neonate with evolving ventilator-associated pneumonia at (A) day 18: right upper lobe collapse (B) day 20: consolidation over the entire right lung.

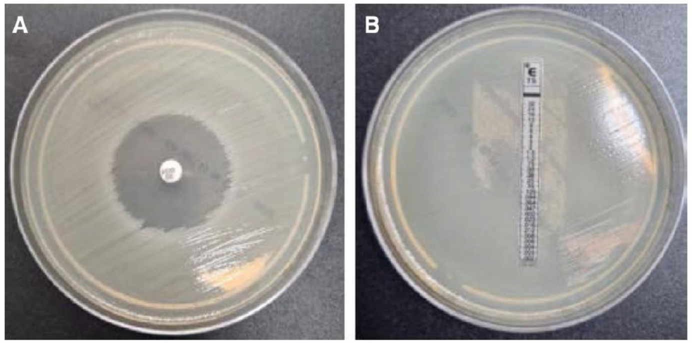
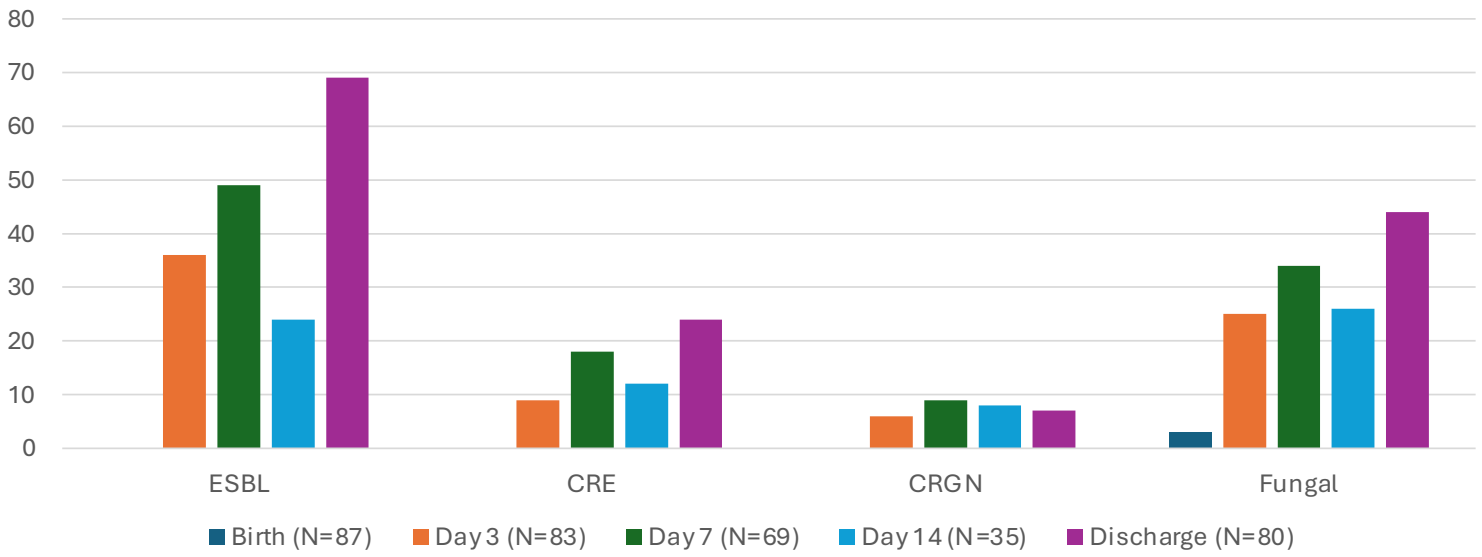


FIGURE 2. Susceptibility testing results for *Stenotrophomonas maltophilia*: (A) disc diffusion with cefiderocol showing susceptibility with a 28 mm zone diameter (B) gradient diffusion (ETEST) with trimethoprim/sulfamethoxazole showing resistance.

The NeoCol Vietnam Study

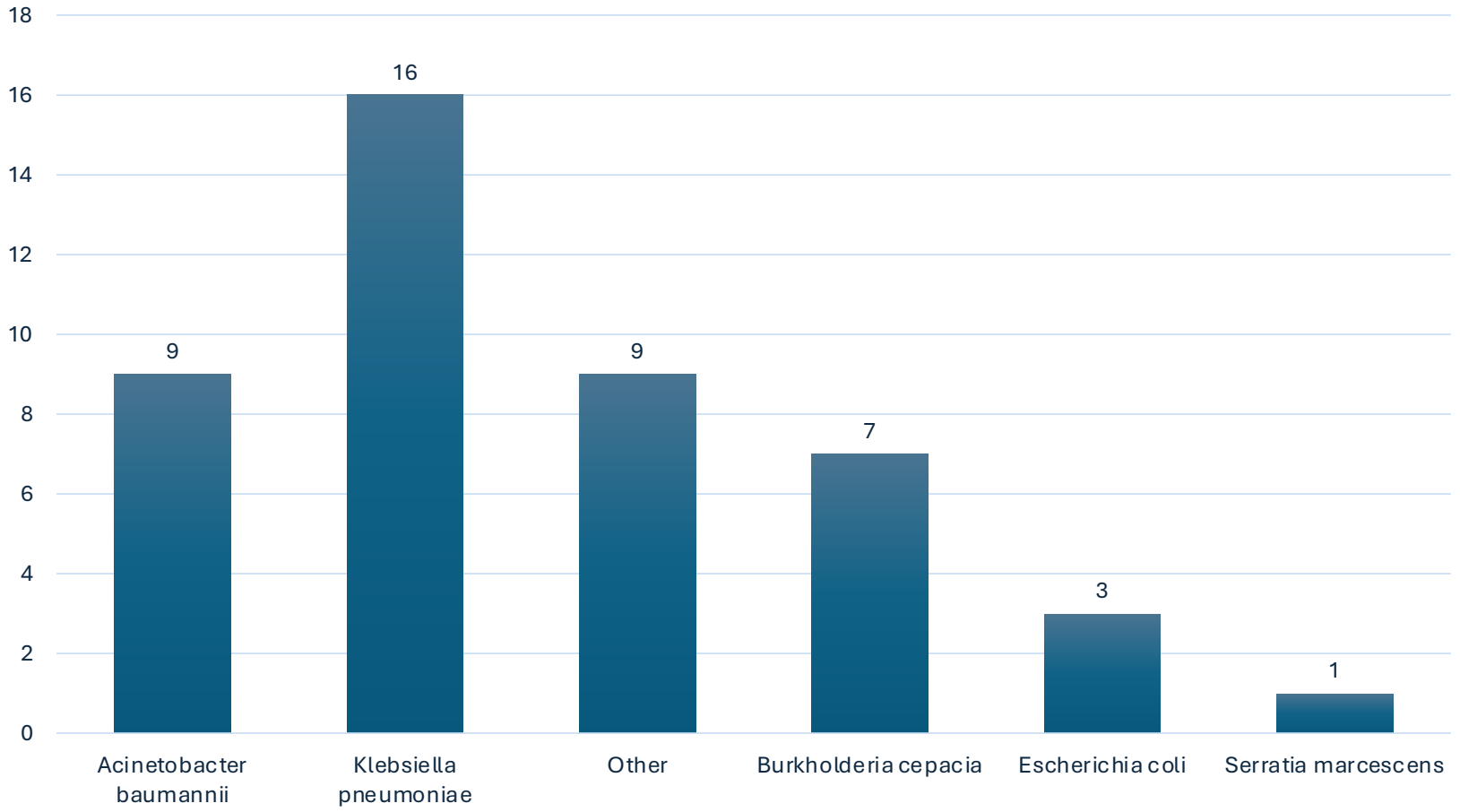
Hung Vuong Hospital, Ho Chi Minh city, Vietnam



	Birth	Day 3	Day 7	Day 14	Discharge
ESBL	0/87	36/83	49/69	24/35	69/80
CRE	0/87	9/83	18/69	12/35	24/80
CRGN	0/87	6/83	9/69	8/35	7/80
Fungal	3/87	25/83	34/69	26/35	44/80

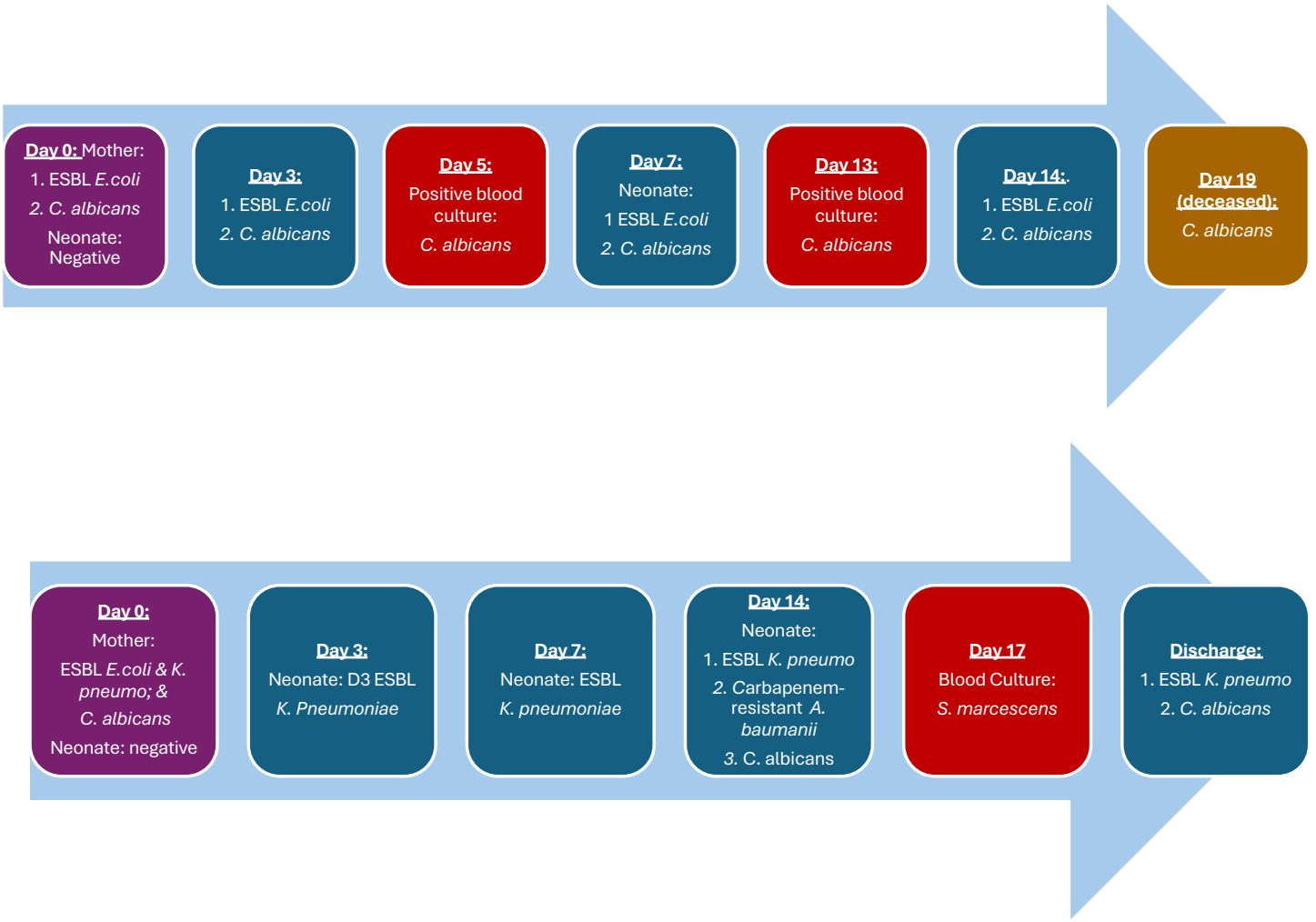
The NeoCol Vietnam Study

Carbapenem-resistant gram-negative bacteria isolated as colonising pathogens



NeoCol Vietnam:

The Relationship between Colonisation and Infection; Vertical & Horizontal Acquisition



The Neonatal Sepsis Management Gap

Empiric Guidelines were curated using data from high-income healthcare settings are are outdated

1990s

GBS + *E. coli* entrenched as primary EOS pathogens (HIC data)

2015-2025

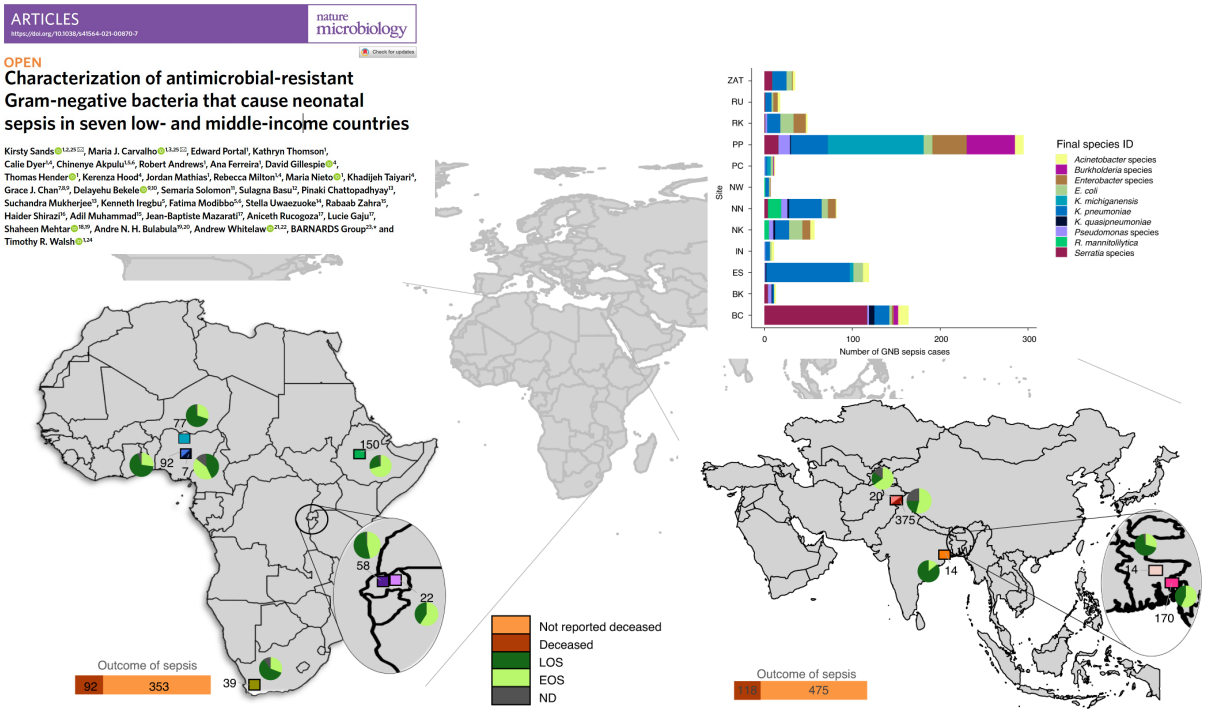
Data from multiple studies focused on high-burden neonatal sepsis countries reveal **high rates of MDR gram-negative infections** as early as day one of life

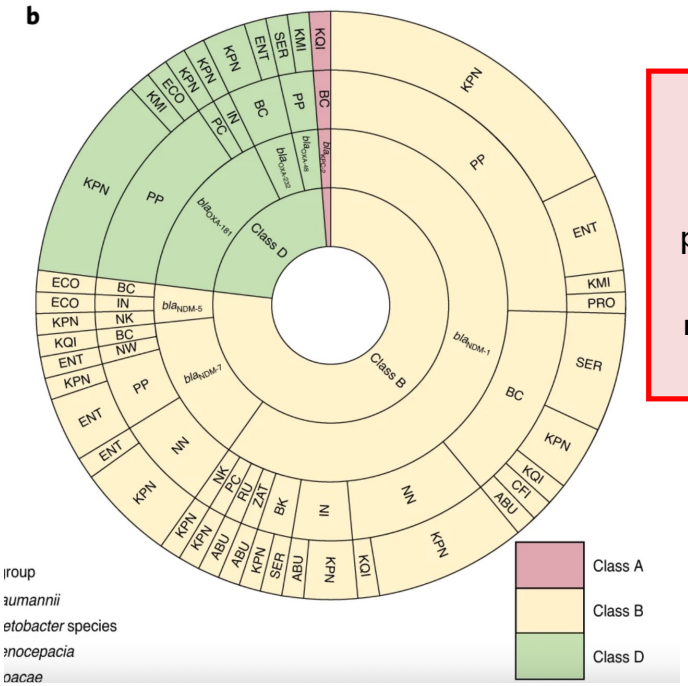
Today

Rising burden of infections due to multidrug-resistant infections:
MBLs predominate

Now, and the Future

Clinicians increasingly need to use broad-spectrum empiric antibiotics → propagates AMR



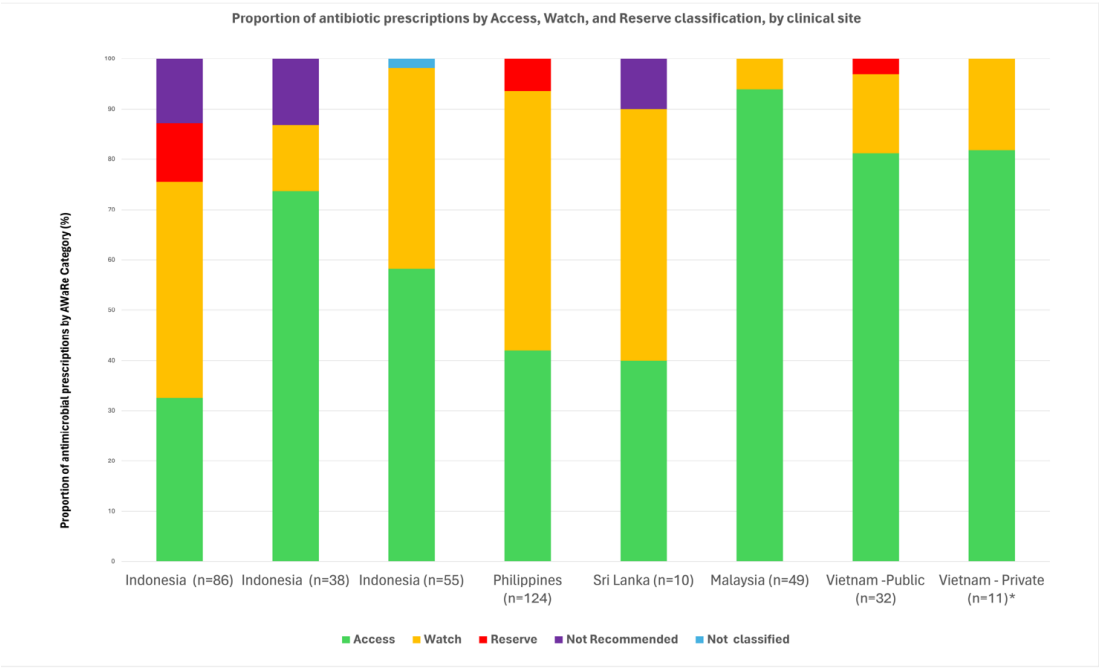


Class B metallo-β-lactamases predominate as causative of neonatal sepsis globally

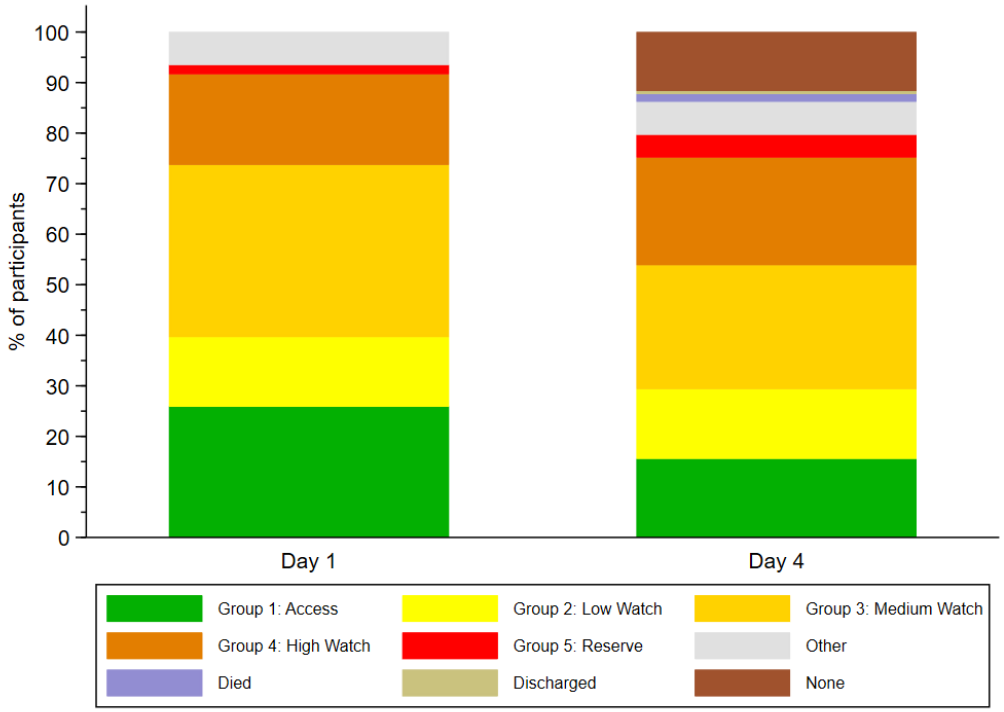
Rapidly rising MDR neonatal infections drives spiraling empiricism

→ High rates of broad-spectrum empiric antibiotic use
→ Drives selection pressure
→ Further propagates AMR

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific



Supplementary Figure 3. Proportion of antibiotic prescriptions by AWaRe Classification by clinical site.
*Vietnam private hospital data pooled secondary to low prescribing frequency.



NeoSEAP study
- High rates of 'Watch' and 'Reserve' antibiotics prescribed
- Evolving carbapenem resistance & colistin resistance in gram-negative pathogens

NeoOBS study: Escalation was common; de-escalation was rare
- Most common empirical therapy combinations prescribed:
  1. Meropenem+vancomycin (n=438, 13.9%)
  2. Ceftazidime+amikacin (n=435, 13.8%)
  3. Piperacillin/tazobactam+amikacin (n=410, 13%)

The Neonatal Sepsis Management Gap

The Antibiotic Pipeline includes very few agents with activity against MBLs, the primary carbapenem resistance mechanism driving neonatal AMR globally

Table 1. Microbiological targets.

	ESBL	KPC	MBL	AmpC	OXA-48	*P. aeruginosa* (MDR/XDR)	*Acinetobacter* (MDR/XDR)	*S. maltophilia*
Aztreonam/avibactam								
Cefepime/enmetazobactam								
Cefepime/taniborbactam								
Cefepime/zidebactam								
Cefiderocol								
Ceftaroline/avibactam								
Ceftolozane/tazobactam								
Ceftazidime/avibactam								
Imipenem/relebactam								
Meropenem/nacubactam								
Meropenem/vaborbactam								

Green = antimicrobial activity, red = no antimicrobial activity, yellow = partial antimicrobial activity, grey = not available. ESBL = extended-spectrum β-lactamase, Ambler Class A β-lactamases; KPC = *Klebsiella pneumoniae* carbapenemase, Ambler Class A β-lactamases; MBL = metallo-β-lactamases, Ambler Class B β-lactamases; AmpC = cephalosporinase, Ambler Class C β-lactamases; OXA-48 = oxicillinase-48, Ambler Class D β-lactamases; MDR = multidrug resistant; XDR = extended drug resistant.

Pincipe *et al.* Pharmaceuticals 2022

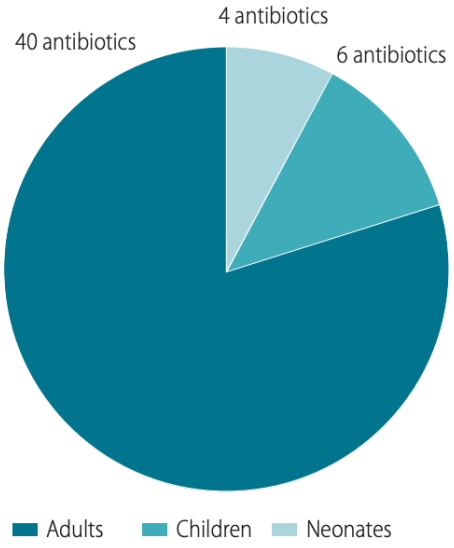
The Research Gap

Only 4 new anti-infectives have been approved for use in neonates this century (v's 44 for adults)

Antibiotics needed to treat multidrug-resistant infections in neonates

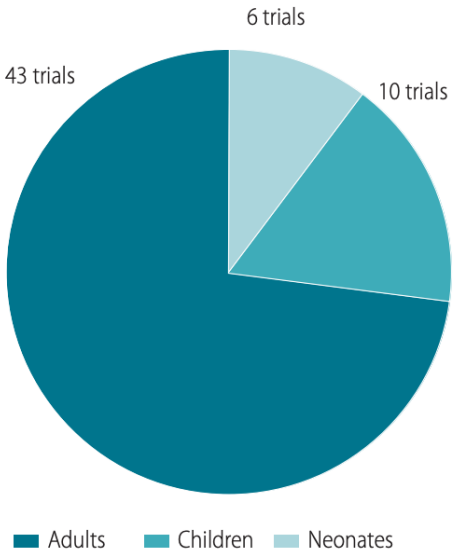
Phoebe CM Williams,[a] Shamim A Qazi,[b] Ramesh Agarwal,[c] Sithembiso Velaphi,[d] Julia A Bielicki,[e] Sumathi Nambiar,[f] Carlo Giaquinto,[g] John Bradley,[h] Gary J Noel,[i] Sally Ellis,[j] Seamus O'Brien,[j] Manica Balasegaram[j] & Michael Sharland[e]

Fig. 1. **Number of antibiotics approved for use since 2000, by age cohort, 2022**



Note: We systematically collated data from the ClinicalTrials.gov database, Food and Drug Administration, European Medicines Agency, PEW Charitable Trusts,[8] World Health Organization[9] and Butler et al.[10,11]

Fig. 2. **Number of antibiotic clinical trials recruiting patients, by age cohort, 2022**

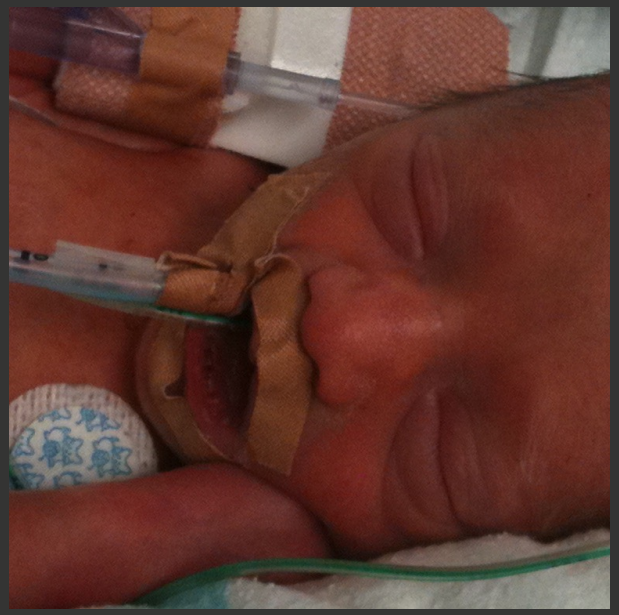


Note: We systematically collated data from the ClinicalTrials.gov database, Food and Drug Administration, European Medicines Agency, PEW Charitable Trusts,[8] World Health Organization[9] and Butler et al.[10,11]

Gates Foundation

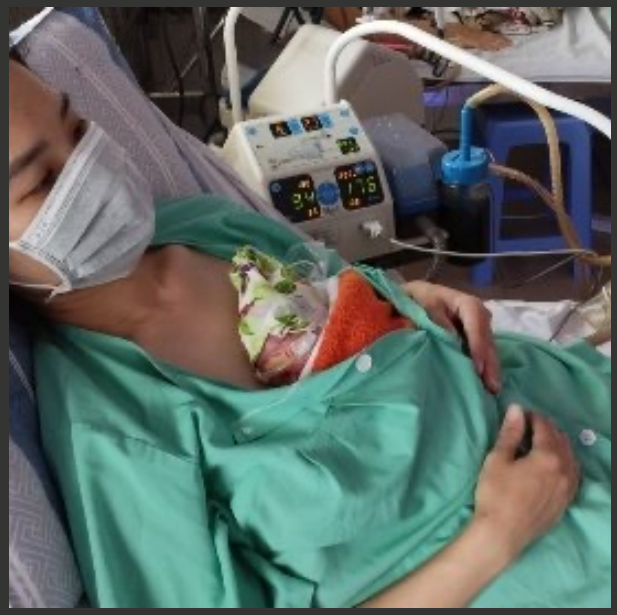
NeoSEAP: The Future

NEOSEAP
Neonatal Sepsis in Southeast Asia and The Pacific



Infection Prevention: The Future

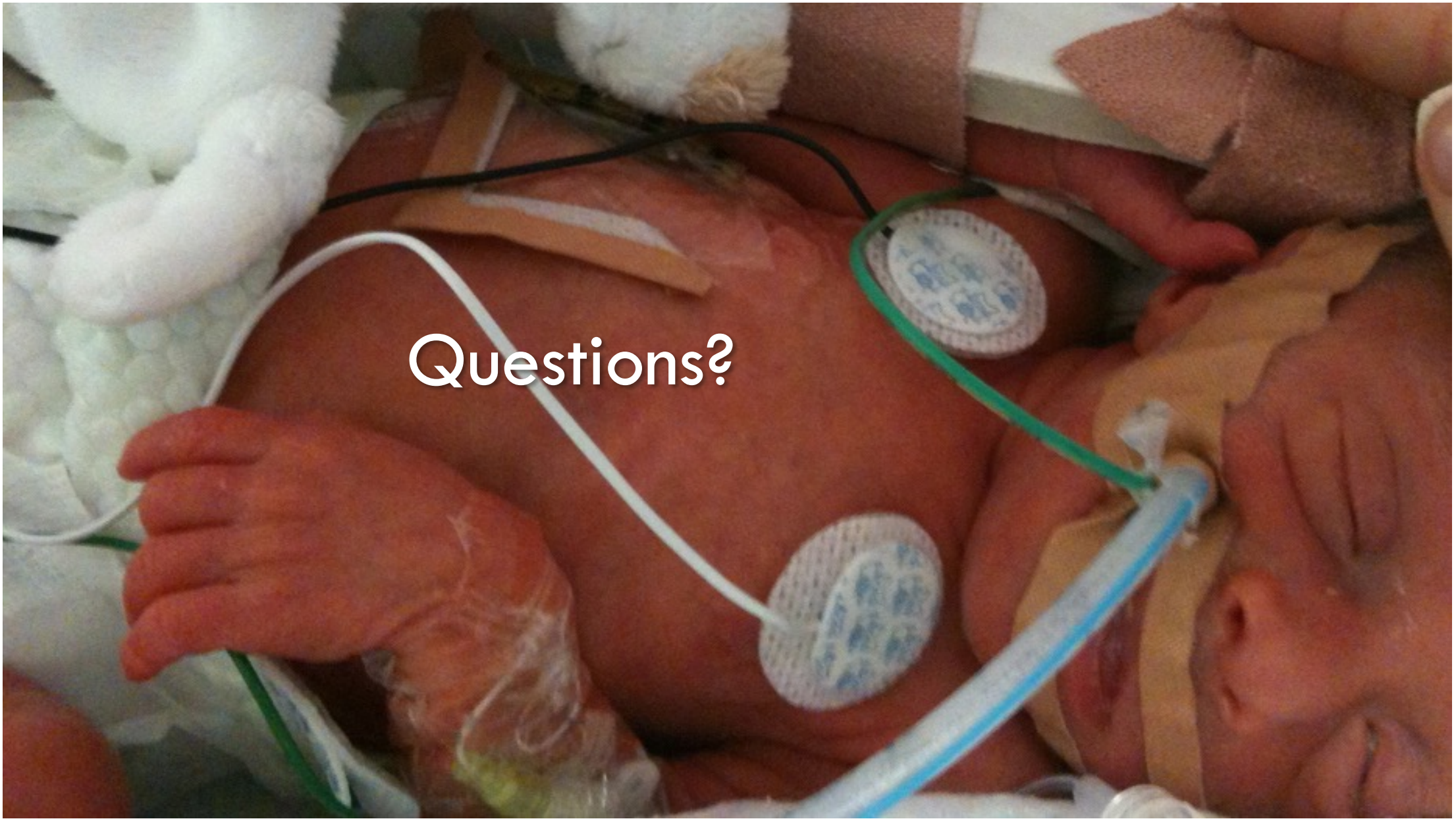
Utilise the data gathered by prospective surveillance to identify a **vaccine** against gram-negative neonatal infections



Infection Prevention: Today

Improve our understanding of the role of the **microbiome** in preventing neonatal infections

Ensure accurate and contemporary data from the Asia Pacific region are in the published literature, and the region is part of the studies that can reduce neonatal sepsis mortality & AMR


Questions?