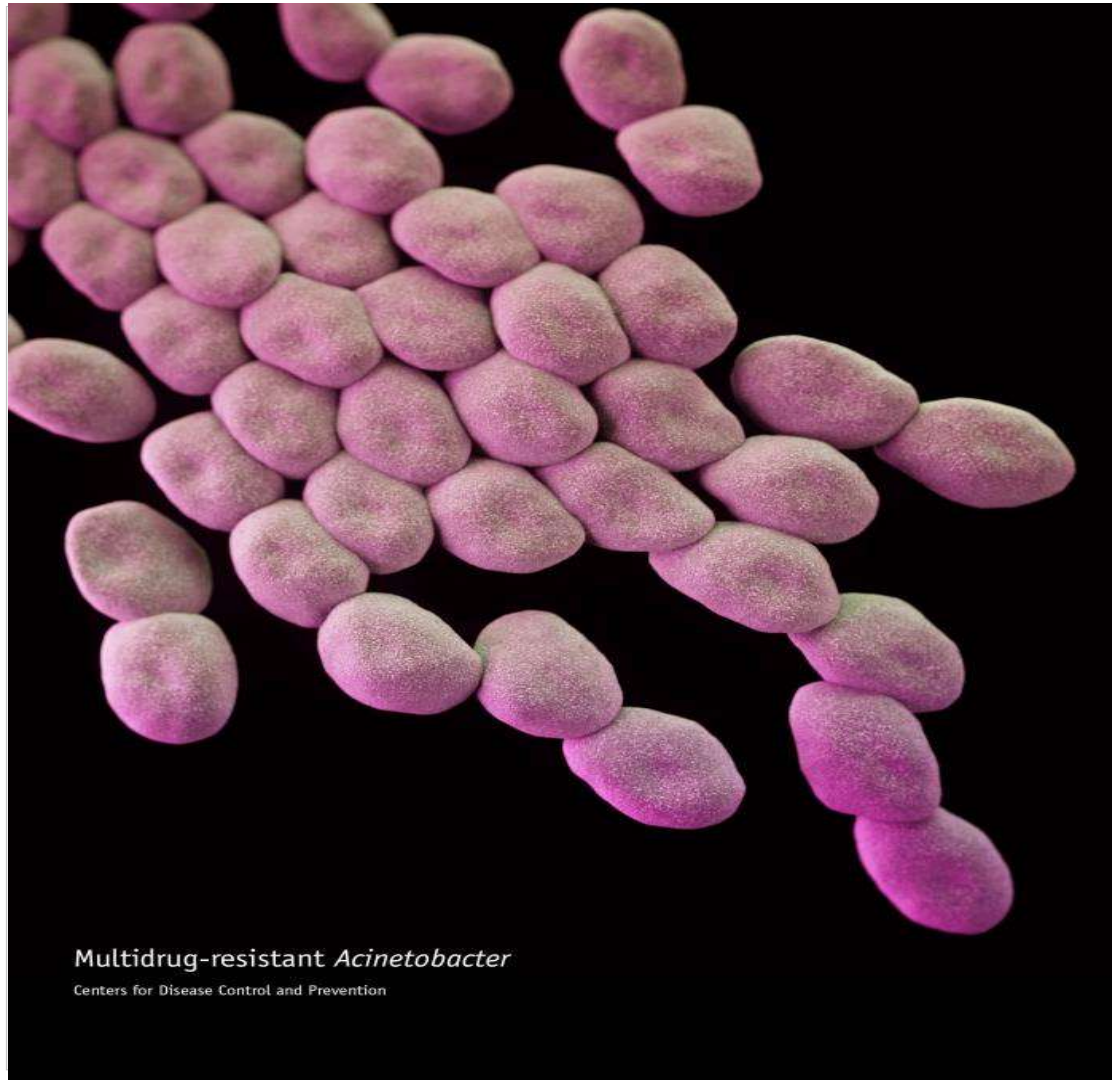


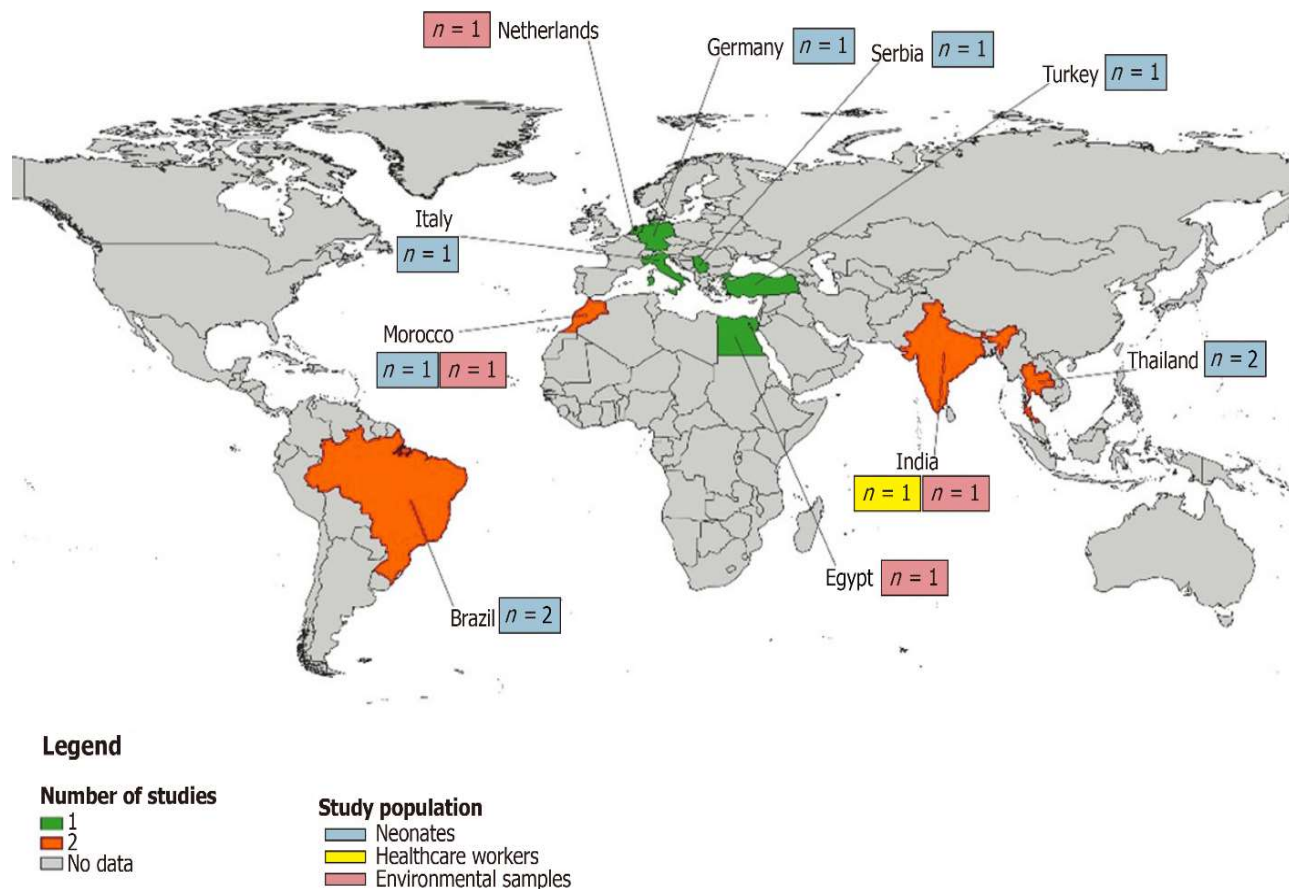


Acinetobacter baumannii: Multidrug- Resistant Pathogen Control Strategies

Your Name & ID Number

Unit: Control of Infectious Disease, BHS022-6

Date of Presentation



(Mbaga et al., 2024)

Introduction & Rationale

Why *A. baumannii*?

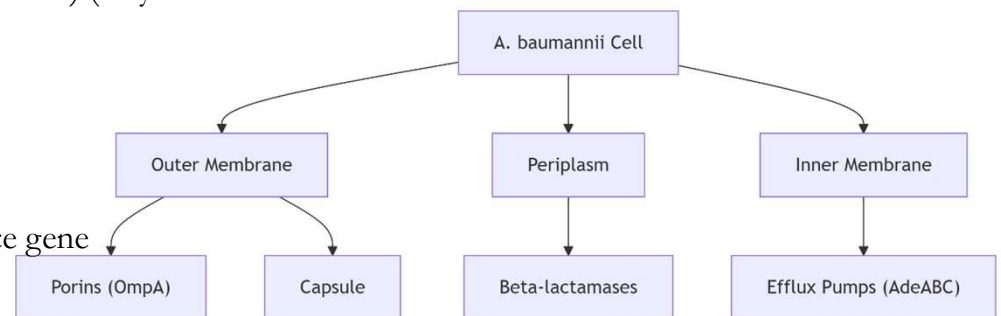
- WHO Critical Priority Pathogen (WHO, 2024)
- ESKAPE pathogen group member
- Mortality rates: 30-75% in ICU infections
- Carbapenem resistance: >60% in some regions (ECDC, 2023)

Key Characteristics:

- Extremely hardy environmental survival (up to 5 months on dry surfaces)
- Rapid acquisition of resistance mechanisms
- Limited treatment options remaining (ECDC, 2023).

Scientific Basis - Causative Agent & Biology

- **Taxonomy:** *Acinetobacter baumannii* (Gram-negative, aerobic coccobacillus)
- **Key Virulence Factors relevant to control:**
 - Biofilm formation (medical device colonization)
 - Capsular polysaccharides (immune evasion)
 - Outer membrane proteins (OmpA - adhesion/invasion)
 - Phospholipases and porins
 - Efflux pumps (AdeABC, AdeIJK - multidrug resistance) (Coyne et al., 2011).
- **Genomic Plasticity:**
 - Large genome (~3.9-4.3 Mbp)
 - High capacity for horizontal gene transfer
 - Abundant insertion sequences promoting resistance gene expression (Coyne et al., 2011).



Pathogenesis & Virulence Factors

◦ Pathogenesis Summary:

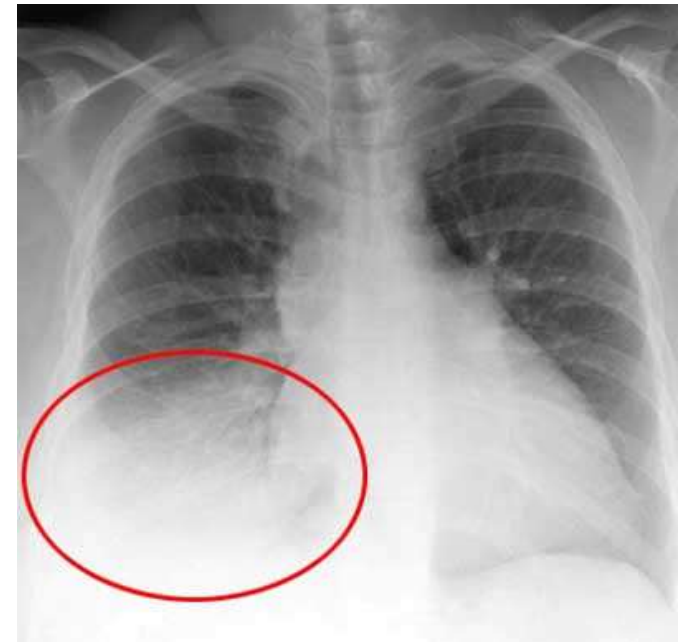
- Opportunistic pathogen - primarily healthcare-associated
- Colonization precedes infection (respiratory tract, wounds, skin)
- Infection types: VAP (ventilator-associated pneumonia), bacteremia, wound infections, UTIs (Wong et al., 2017).

◦ Key Virulence Mechanisms:

- Iron acquisition systems (siderophores - acinetobactin, baumannoferrin)
- Type VI secretion system (T6SS) - bacterial competition
- Lipopolysaccharide (LPS) - endotoxin activity
- Phospholipase D (cleavage of host cell membranes) (Wong et al., 2017).

◦ Clinical Significance:

- Mortality: 30-75% depending on resistance profile
- Prolonged hospitalization (average +15-20 days)
- High economic burden (€20,000-40,000 per case in Europe) (Wong et al., 2017).



Modes of Transmission & Epidemiology

Transmission Dynamics:

Primary: Healthcare-associated (patient-to-patient via healthcare workers' hands)

Secondary: Environmental surfaces (bed rails, sinks, ventilators, curtains)

Rare: Community-acquired (tropical regions, war wounds) (CDC, 2024)

Epidemiological Data (Global):

CRAB rates: Middle East (70-85%), Southern Europe (40-60%), USA (30-50%), Asia (50-75%)

Outbreak settings: ICUs, burn units, long-term care facilities (CDC, 2024)

Risk Factors for Acquisition:

ICU admission (OR 5.2, 95% CI 3.1-8.7)

Mechanical ventilation (OR 4.8)

Previous carbapenem use (OR 6.3)

Length of stay >7 days (CDC, 2024)

Current Control Methods - Infection Prevention

Standard + Contact Precautions:

- Single rooms or cohorting
- Dedicated equipment
- Enhanced environmental cleaning (Biswas, Tiwari and Tiwari, 2019).

Environmental Decontamination:

- Sporicidal agents (chlorine-based, hydrogen peroxide)
- UV-C disinfection (terminal cleaning)
- Hydrogen peroxide vapor (HPV) (Biswas, Tiwari and Tiwari, 2019).

Hand Hygiene:

- Alcohol-based hand rub (ABHR)
- effective but requires compliance >70%
- Soap and water when visibly soiled (Biswas, Tiwari and Tiwari, 2019).

Surveillance:

- Active screening (rectal, respiratory, wound swabs)
- Molecular testing (PCR for carbapenemase genes - blaOXA-23, blaOXA-24/40, blaNDM) (Biswas, Tiwari and Tiwari, 2019).

Decolonization:

- Limited evidence base
- Chlorhexidine bathing (controversial - possible resistance emergence) (Biswas, Tiwari and Tiwari, 2019)

Current Control Methods - Antimicrobial Treatment



Last-Line Agents (Limited options):

- Colistin (polymyxin E) - nephrotoxicity ~40-60%, heteroresistance common
- Tigecycline (glycylcycline) - not for bacteremia (low serum levels)
- Sulbactam-durlobactam (XACDURO®) - FDA approved 2023, specifically for CRAB
- Cefiderocol (siderophore cephalosporin) - variable efficacy (Karruli et al., 2023)

Combination Therapy (Debated):

- Colistin + carbapenem (controversial)
- Colistin + tigecycline + meropenem (triple therapy)
- Colistin + sulbactam (Karruli et al., 2023).

Pharmacokinetic/Pharmacodynamic Challenges:

- Poor lung penetration (tigecycline)
- Nephrotoxicity limiting colistin dosing
- Emerging resistance during therapy (Karruli et al., 2023)



Critical Evaluation of Literature - Strengths

◦ High-Quality Evidence Available:

- Randomised controlled trials: sulbactam-durlobactam (Innoviva, 2023)
- Large cohort studies: carbapenem-resistant outcomes (Lai et al., 2024)
- Systematic reviews: infection control bundles (Meschiari et al., 2021)

◦ Methodological Strengths:

- Multicentre RCTs with rigorous outcomes
- Genomic characterisation of resistance mechanisms
- Meta-analyses with low heterogeneity in selected subgroups (Innoviva, 2023)

Strengths of Current Literature:

Aspect	Strength
Molecular epidemiology	WGS enables precise outbreak tracking
Surveillance networks	ECDC, CDC, WHO GLASS provide comparable data
New drug development	Validated regulatory pathways (FDA LPAD)
Implementation science	Real-world effectiveness studies

Critical Evaluation of Literature - Limitations

◦ **Specific Problems:**

- Colistin studies: inconsistent definitions, variable dosing, retrospective designs
- Decolonisation research: no high-quality RCTs, conflicting results
- Environmental disinfection: surrogate outcomes (colony counts) not patient outcomes
- Combination therapy: meta-analyses show contradictory conclusions (Boutzoukas and Doi, 2025).

◦ **Geographic Bias:**

- Most RCTs from high-income countries (USA, Germany, France)
- Limited data from high-burden settings (Middle East, Southeast Asia) (Boutzoukas and Doi, 2025).

Major Limitations & Gaps:

Limitation	Impact
Small sample sizes	Underpowered for mortality differences
Heterogeneous study populations	Limited generalisability
Lack of blinded RCTs for infection control	High risk of bias
Publication bias	Overestimation of intervention effects
Short follow-up duration	Missed long-term outcomes

Evaluation of Specific Agents for Treatment/ Control

Treatment Agents (Clinical Use):

Agent	Mechanism	Position in Therapy	Evidence Grade
Sulbactam-durlobactam	Beta-lactamase inhibitor	First-line for CRAB	High (RCT)
Colistin	Membrane disruption	Second-line (toxicity)	Low-moderate
Cefiderocol	Siderophore cephalosporin	Salvage therapy	Moderate
Tigecycline	30S ribosome inhibitor	Pneumonia only	Low-moderate
Eravacycline	Tetracycline analogue	Limited data	Low

Control Agents (Environmental/Decolonisation):

Chlorhexidine: Topical decolonisation (emerging resistance)

Sodium hypochlorite (bleach): Environmental disinfection (1000-5000ppm)

Hydrogen peroxide vapor: Terminal room disinfection

UV-C light: Surface decontamination (254nm)

Bacteriophages: Experimental decolonisation (clinical trials ongoing) (Innoviva, 2023).

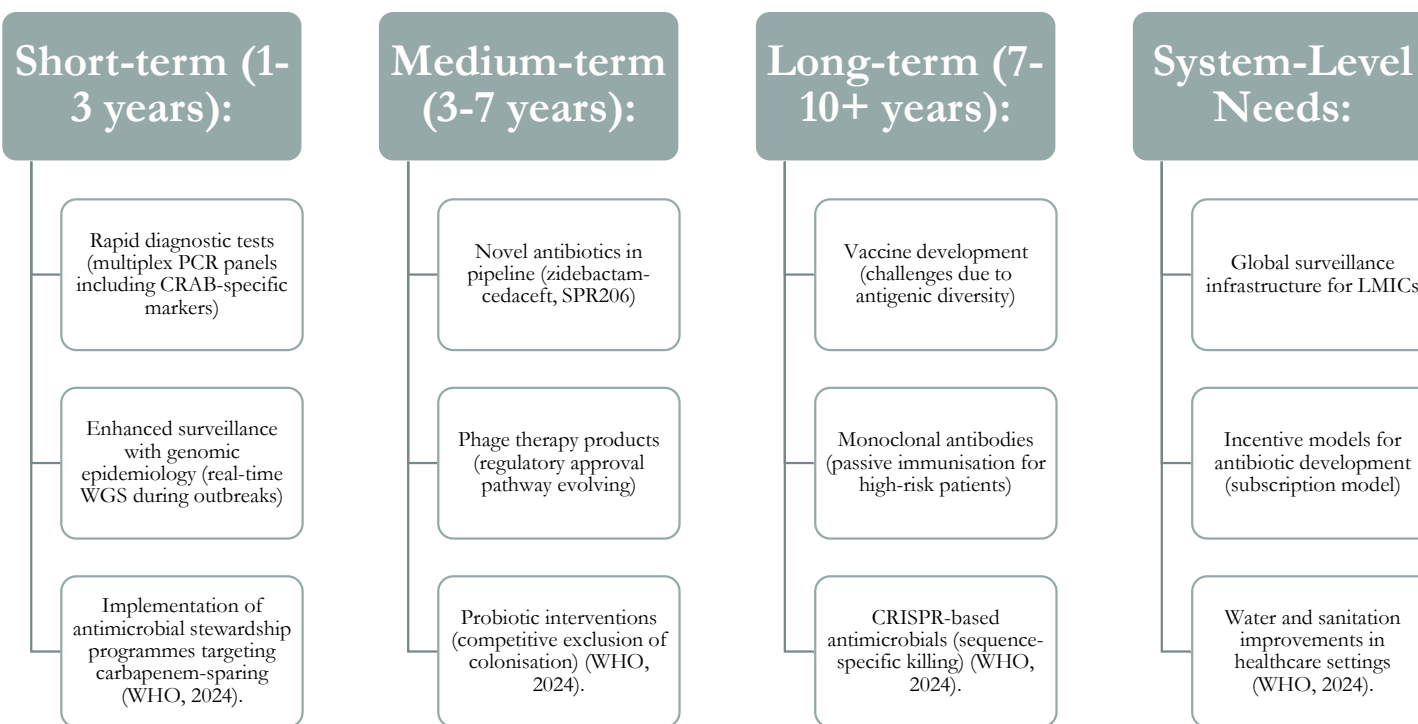
Emerging Agents in Development:

Phage therapy (clinical trials NCT04556318, NCT04636554)

Novel siderophore conjugates

Anti-virulence strategies (biofilm inhibitors, T6SS inhibitors) (Innoviva, 2023).

Future Developments in Control



Reference list

- Biswas, D., Tiwari, M. and Tiwari, V. (2019). Molecular mechanism of antimicrobial activity of chlorhexidine against carbapenem-resistant *Acinetobacter baumannii*. *PLOS ONE*, 14(10), p.e0224107. doi: <https://doi.org/10.1371/journal.pone.0224107>.
- Boutzoukas, A. and Doi, Y. (2025). The global epidemiology of carbapenem-resistant . *PubMed*, [online] 7(4), pp.dlaf134–dlaf134. doi:<https://doi.org/10.1093/jacamr/dlaf134>.
- CDC (2024). *Antimicrobial Resistance Threats in the United States, 2021-2022*. [online] Centers for Disease Control and Prevention. Available at: <https://www.cdc.gov/antimicrobial-resistance/data-research/threats/update-2022.html>.
- Coyne, S., Courvalin, P. and Périchon, B. (2011). Efflux-mediated antibiotic resistance in *Acinetobacter* spp. *Antimicrobial agents and chemotherapy*, [online] 55(3), pp.947–53. doi: <https://doi.org/10.1128/AAC.01388-10>.
- ECDC (2023). *Antimicrobial resistance surveillance in Europe 2023 - 2021 data*. [online] www.ecdc.europa.eu. Available at: <https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-surveillance-europe-2023-2021-data>.
- Innoviva (2023). *Results from Pivotal Phase 3 ATTACK Trial of Investigational Sulbactam-Durlobactam for Treatment of Serious Infections Caused by Acinetobacter Published in The Lancet Infectious Diseases*. [online] <https://innovivaspecialtytherapeutics.com/results-from-pivotal-phase-3-attack-trial-of-investigational-sulbactam-durlobactam-for-treatment-of-serious-infections-caused-by-acinetobacter-published-in-the-lancet-infectious-diseases/> [Accessed 19 Apr. 2026].
- Karruli, A., Migliaccio, A., Pournaras, S., Durante-Mangoni, E. and Zarilli, R. (2023). Cefiderocol and Sulbactam-Durlobactam against Carbapenem-Resistant *Acinetobacter baumannii*. *Antibiotics*, [online] 12(12), pp.1729–1729. doi: <https://doi.org/10.3390/antibiotics12121729>.
- Lai, C., Ma, Z., Zhang, J., Wang, J., Wang, J., Wu, Z. and Luo, Y. (2024). Efficiency of combination therapy versus monotherapy for the treatment of infections due to carbapenem-resistant Gram-negative bacteria: a systematic review and meta-analysis. *Systematic Reviews*, 13(1). doi: <https://doi.org/10.1186/s13643-024-02695-x>.
- Mbagi, D.S., Kenmoe, S., Esemu, S.N., Bowo-Ngandji, A., Kench, N.K., Akoachere, J.-F.T.K., Gonsu, H.K., Ndip Ndip, R., Ebogo-Belobo, J.T., Kengne-Ndé, C., Tendongfor, N., Assam Assam, J.P., Ndip, L.M., Bikoï, J.N. and Essama, S.H.R. (2024). Epidemiology of carbapenem-resistant *Acinetobacter baumannii* colonization in neonatal intensive care units: A systematic review and meta-analysis. *World Journal of Meta-Analysis*, 12(1). doi: <https://doi.org/10.13105/wjma.v12.i1.90229>.
- Meschieri, M., López-Lozano, J.-M., Di Pilato, V., Gimenez-Esparza, C., Vecchi, E., Bacca, E., Orlando, G., Franceschini, E., Sarti, M., Pecorari, M., Grottola, A., Venturelli, C., Busani, S., Serio, L., Girardis, M., Rossolini, G.M., Gyssens, I.C., Monnet, D.L. and Mussini, C. (2021). A five-component infection control bundle to permanently eliminate a carbapenem-resistant *Acinetobacter baumannii* spreading in an intensive care unit. *Antimicrobial Resistance & Infection Control*, 10(1). doi: <https://doi.org/10.1186/s13756-021-00990-z>.
- WHO (2024). *Global Antimicrobial Resistance and Use Surveillance System (GLASS)*. [online] World Health Organization. Available at: <https://www.who.int/initiatives/glass>.
- Wong, D., Nielsen, T.B., Bonomo, R.A., Pantapalangkoor, P., Luna, B. and Spellberg, B. (2017). Clinical and Pathophysiological Overview of *Acinetobacter* Infections: a Century of Challenges. *Clinical Microbiology Reviews*, [online] 30(1). doi: <https://doi.org/10.1128/cmr.00058-16>.



Thank You