5-12-2023

A Systematic Review: Examining Waterborne Acinetobacter baumannii Outbreaks in Hospitals

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Recommended Citation
Bushey, Jessica, "A Systematic Review: Examining Waterborne Acinetobacter baumannii Outbreaks in Hospitals." Thesis, Georgia State University, 2023.
doi: https://doi.org/10.57709/35483323

ABSTRACT

A Systematic Review: Examining Waterborne *Acinetobacter baumannii* Outbreaks in Hospitals

By

Jessica H. Bushey

April 12, 2023

INTRODUCTION: *Acinetobacter baumannii* (*A. baumannii*) causes the most human infections of any *Acinetobacter* species and has become a concerning cause of healthcare-associated infections. Further review of its role in water-related hospital outbreaks is needed to better understand the burden of *A. baumannii* on healthcare systems.

AIM: This review sought to examine water-related outbreaks caused by *A. baumannii* in hospitals since 2006. The review aimed to identify and analyze the reservoirs, antimicrobial susceptibility, and infection control practices of *A. baumannii* associated outbreaks to better understand effective prevention and control measures.

METHODS: This systematic review followed the guidelines from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA). Three databases were searched including EMBASE, PubMED, and Web of Science. Data was extracted using a data extraction sheet focused on reservoirs, antimicrobial susceptibility, and infection control practices.

RESULTS: A total of seven outbreaks of *A. baumannii* within different hospital settings were examined. Every outbreak involved drug resistant strains of *A. baumannii* and required enhanced or novel infection control interventions. The hospital reservoirs varied between facilities, and no two outbreak strains were susceptible to the same forms of treatment.

DISCUSSION: With increasing antimicrobial resistance, identifying effective treatment and infection control practices are vital for preventing and controlling *A. baumannii* outbreaks. Global best practices are needed to combat this pathogen, and recommendations should be based on the most current evidence.

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by

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A Thesis Submitted to the Graduate Faculty
of Georgia State University in Partial Fulfillment
of the
Requirements for the Degree

MASTER OF PUBLIC HEALTH

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APPROVAL PAGE

A Systematic Review: Examining Waterborne *Acinetobacter baumannii* Outbreaks in Hospitals

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Acknowledgments

I would like to acknowledge the support of my family, especially my husband. I also want to acknowledge the flexibility and understanding provided by my colleagues at Cobb and Douglas Public Health. Thank you to the Georgia State University Library staff for assisting me with this research. Finally, I would like to thank Dr. Casanova and Dr. Stauber for supporting me with this project.

Author's Statement Page

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Jessica H. Bushey

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1 INTRODUCTION

1.1 Background

The bacterial species *Acinetobacter*, often found in soil and water, can lead to severe human infections. *Acinetobacter baumannii* (*A. baumannii*), the species which causes the most human infections, is a gram-negative bacillus deemed a priority pathogen by the World Health Organization (WHO) (*Acinetobacter in Healthcare Settings | HAI | CDC*, 2019; *WHO Publishes List of Bacteria for Which New Antibiotics Are Urgently Needed*, n.d.). As an opportunistic pathogen, *A. baumannii* has become a concerning cause of healthcare-associated infections over the past few years and is commonly implicated in outbreaks at healthcare facilities. Patients who are immunocompromised, experience prolonged hospital stays, require devices such as ventilators, catheters, and sutures, or have open wounds are at an increased risk for infection (Centers for Disease Control and Prevention [CDC], 2019). *A. baumannii* can infect the blood, lungs, respiratory tract, urinary tract, skin, wounds, and even the eyes (Howard et al., 2012). *A. baumannii* may colonize patients without producing any symptoms or signs of infection. Unfortunately, *A. baumannii* is considered the most resistant *Acinetobacter* species, as it has developed resistance to nearly all antibiotics (Looveren & Goossens, 2004; Singh et al., 2022).

In 2019, The Centers for Disease Control and Prevention (CDC) escalated the threat level for *A. baumannii* from serious to urgent. In 2017 alone, *A. baumanni* was responsible for an estimated 8,500 cases in hospitals and 700 deaths. This led to an estimated attributable healthcare cost of $281 million (CDC, 2019). Since 2017, *A. baumannii* has continued to infect hospitalized patients, even causing outbreaks during the SARS-COV-2 pandemic, furthering the strain on the healthcare system (Thoma et al., 2022). Not only is *A. baumannii* considered a multidrug-resistant organism (MDRO), there is currently no known effective monotherapy, and infections are often associated with high mortality rates (Karakonstantis et al., 2021).

This systematic review will address the most current details known about *A. baumannii* through examination of water-related outbreaks in hospital settings and will provide updated information surrounding reservoirs, treatment, prevention, and control measures.

1.2 Classification

The genus *Acinetobacter* is comprised of at least 32 genomic species, of which at least 23 have been assigned species names (Lin & Lan, 2014; Looveren & Goossens, 2004). The *Acinetobacter* genus is an aerobic gram-negative coccobacillus that is glucose-non-fermentative, non-fastidious, catalase-positive, and oxidase-negative. It also happens to be non-motile and occurs most often in diploid formation or chains (Lin & Lan, 2014; Looveren & Goossens, 2004).

1.3 Reservoirs and Survival in the Environment

Acinetobacter species are ubiquitous in soil and water (Lin & Lan, 2014). However, the reservoirs for *A. baumannii* in the environment have required more extensive investigation. According to Eveillard et al., in a study performed in Hong Kong, *A. baumannii* accounted for 23% of the *Acinetobacter* species found in soil samples (2013). Additionally, *A. baumannii* has been found in wounds of survivors of natural disasters, such as earthquakes and tsunamis (Eveillard et al., 2013). With its presence in soil, *A. baumannii* has been isolated from fruits and vegetables, including in settings such as grocery stores and in private gardens (Eveillard et al., 2013). Other foods include meat from butchers and supermarkets, fish from aquaculture, raw cow milk at dairy farms, and raw cheese from butchers and shops (Carvalheira et al., 2021). Furthermore, *A. baumannii* has been isolated from animals, including horses, pigs, cattle, human head and body lice, and domesticated pets (Eveillard et al., 2013). Therefore, it is reasonable that *A. baumannii* has been found in manure, agricultural soil, and even fish and shrimp farms (Eveillard et al., 2013).

The presence of *A. baumannii* in manure is significant, as it can be further spread throughout the environment in livestock wastewater. Pulami et al., examined the diversity of *Acinetobacter* species as they relate to livestock and human wastewater (2023). The authors identified 52 isolates of *A. baumannii* from raw and digested manure and wastewater treatment plants. Some of these plants received human hospital wastewater, as well as veterinarian wastewater from veterinary clinics. The authors were able to determine through a comparative study of phylogenetic analysis and multi-locus sequence typing that some of the urban wastewater treatment plants receiving hospital water were releasing clinically relevant and resistant strains of *Acinetobacter* bacteria into the environment (Pulami et al., 2023).

Beyond environmental sources, the hospital and other healthcare facilities are an important reservoir for *A. baumannii*, for *A. baumannii* is reported as causing the most outbreaks in clinical settings of all the *Acinetobacter* species (Lin & Lan, 2014; Looveren & Goossens, 2004). While it has been determined that *A. baumannii* can survive for long durations on inanimate surfaces, *Acinetobacter* species have been associated with transmission through hospital water as well (Decker & Palmore, 2013; Kramer et al., 2006). Within healthcare facilities, *A. baumannii* has been isolated from sinks, hydrotherapy pools, drains, faucets, and showers (Carvalheira et al., 2021; Kizny Gordon et al., 2017; Kramer et al., 2006).

The ability of *A. baumannii* to form biofilms and survive in low nutrient conditions has led to an increased risk for environmental colonization (Kizny Gordon et al., 2017). Unfortunately, *A. baumannii* associated outbreaks may be underestimated due to lack of diagnoses outside clusters, along with outbreak assessments not including investigations of the healthcare water environment (Decker & Palmore, 2013; Kizny Gordon et al., 2017).

Furthermore, *A. baumannii* is associated with both human colonization and asymptomatic carriage. *A. baumannii* has been found to colonize the skin, respiratory tract, and the digestive tract (Looveren & Goossens, 2004). Eveillard et al. details community carriage on skin in several studies, including on the hands of residents in New York City and the skin on foreheads and feet of nondeployed United States' soldiers (2013). The ability of *A. baumannii* to colonize skin may contribute to transmission in healthcare settings through the contamination of healthcare workers' hands (Looveren & Goossens, 2004).

1.4 Methods of Detection

Identifying *Acinetobacter* species is vital to understanding the survival and implications of *Acinetobacter* reservoirs. Identification is also of particular importance in the hospital setting so that facilities may respond appropriately to outbreaks in a timely manner. Multiple forms of molecular sequencing and molecular fingerprinting have been developed that aid in identifying *Acinetobacter* species. These include pulsed-field gel electrophoresis (PFGE), polymerase chain reaction (PCR)-based fingerprinting techniques like random amplified polymorphic DNA analysis and repetitive extragenic palindromic sequence-based PCR (rep-PCR), ribotyping, RNA spacer fingerprinting, amplified ribosomal DNA restriction analysis, multi-locus sequence typing (MLST), and amplified fragment length polymorphism analysis. Some recent methods of sequence analysis include ribosomal intergenic spacer, 16S-23S rRNA gene regions, rpoB gene and gyrB gene sequence analyses (C.-R. Lee et al., 2017; Lin & Lan, 2014).

1.5 Disease and Antimicrobial Resistance

A. baumannii is responsible for both community-acquired infections and hospital-acquired infections. This bacteria causes pneumonia (including ventilator-associated), urinary tract infections, bacteremia, wound infections, and meningitis (Lin & Lan, 2014). According to Lin and Lan (2014), reports of community-acquired infections are on the rise and have been associated with wound infections following natural disasters. Community-acquired pneumonia due to *A. baumannii* infection have also increased, notably during warmer months (Eveillard et al., 2013).

Despite increases in reports of community-acquired infection, most *A. baumannii* infections are associated with nosocomial spread and are highly implicated in outbreaks within intensive care units. Unfortunately, the ability of *Acinetobacter* to colonize humans makes it difficult to estimate the true spread within a facility if only symptomatic patients are tested. Additional factors increasing the risk for infection include hospitalization, mechanical ventilation, co-morbidities such as cardiovascular or respiratory disease, previous infections and antibiotic use, as well as the presence of indwelling catheters (Looveren & Goossens, 2004).

The primary treatment for active *A. baumannii* infection is antibiotics. However, *A. baumannii* is the most antibiotic resistant of all *Acinetobacter* species, and currently, no effective monotherapy exists. For this reason, susceptibility testing is recommended prior to administering antibiotics (Tamma et al., 2022). Once susceptibility results are received, the Infectious Diseases Society of America (IDSA) suggests ampicillin-sulbactam presuming susceptibility. Otherwise, minocycline, tigecycline, polymyxin B (colistin for cystitis), or cefiderocol are suggested with at least two agents in combination therapy for moderate to severe infections (Tamma et al., 2022). However, it is important to note that comparing susceptibility rates to different antibiotics is difficult with the variations between local epidemiology, study protocols, and differences in patient populations and selective pressures (Looveren & Goossens, 2004). *Acinetobacter* seems to have a propensity for developing resistance quickly, which is believed to stem from evolutionary exposure to organisms within soil who produce antibiotics. As a result, *Acinetobacter* resistance to antimicrobial agents include aminoglycosides, beta-lactams, and quinolones; it is also becoming increasingly resistant to last line treatments, including colistin and carbapenems (Ibrahim et al., 2021; Looveren & Goossens, 2004). Multidrug-resistant *A. baumannii* is the result of multiple mechanisms, such as acquiring mobile genetic elements like transposons, plasmids, and integrons (Ibrahim et al., 2021). CDC's Antibiotic Resistance Threat Report from 2019 demonstrated trends in resistance for *A. baumannii*, such as the percentage of carbapenem-resistant *A. baumannii* complex (CRAB) isolates that tested non-susceptible to certain antibiotics, which are outlined in Table 1. These isolates were obtained through CDC's Emerging Infections Program (CDC, 2019). Further examination is needed to discern which treatments have been most effective in recent outbreaks.

Table 1. Percent of CRAB Isolates Not Susceptible to Certain Antibiotics

Select Antibiotics	2013	2014	2015	2016	2017
Any fluoroquinolone	98%	93%	97%	92%	89%
Any extended-spectrum β-lactam	80%	75%	81%	79%	75%
Ampicillin/Sulbactam	62%	62%	59%	64%	61%
Trimethoprim/sulfamethoxazole	84%	74%	81%	77%	66%

1.6 Guidelines and Monitoring

Because of *A. baumannii's* concerning antimicrobial resistance and increasing threat to healthcare, CRAB is included in surveillance through CDC's Emerging Infection Program's (EIP) Multi-site Gram-negative Surveillance Initiative (MugSI). CRAB includes *A. baumannii*, *A. baumannii* complex, and *A. calcoaceticus-baumannii* complex. MugSI uses population and laboratory-based surveillance to determine spread and trends of gram-negative bacteria. The surveillance also aims to evaluate incidence, determine characteristics, and describe resistance mechanisms (*MuGSI | HAIC Activities | HAI | CDC*, 2023). For CRAB to meet the case definition, specimens must be collected from either a normally sterile site, urine, lower respiratory tract, or a wound. Surveillance areas of MugSI are limited to California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee (*MuGSI | HAIC Activities | HAI | CDC*, 2023). Case rates and death rates for CRAB between 2012 and 2018 calculated from MugSI are demonstrated in Table 2 and Figure 1.

Table 2. Case Rates and Death Rates for CRAB from 2012-2018

Year	Cases per 100,000 population	Deaths per 100,000 population
2012	1.58	0.32
2013	1.39	0.22
2014	1.04	0.2
2015	1.1	0.16
2016	0.76	0.07
2017	0.8	0.18
2018	0.53	0.08

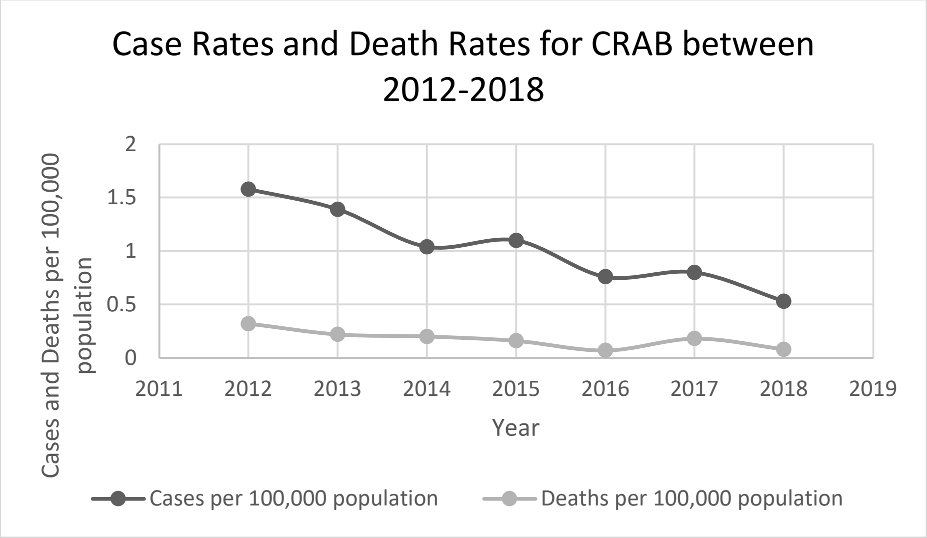

Figure 1. CRAB Case Rates and Death Rates between 2012-2018 from MugSI

While the overall case rates and death rates are trending down, CDC maintains *A. baumannii* as an urgent threat mainly due to its antimicrobial resistance as previously discussed (CDC, 2019).

Several sources exist to provide guidelines and monitoring for resistant strains of *A. baumannii*. The IDSA has published the Guidance on The Treatment of Antimicrobial-Resistant Gram-Negative Infections: Version 2.0. This guidance provides recommendations for the management and treatment of CRAB (Tamma et al., 2022). Additionally, the Association for Professionals in Infection Control and Epidemiology (APIC) released the Guide to Elimination of Multidrug-resistant *Acinetobacter baumannii* Transmission in Healthcare settings in 2010 (“Implementation Guides,” n.d.).

2 METHODS and PROCEDURES

2.1 Search Strategy

The purpose of this systematic review was to 1) Identify *A. baumannii* outbreaks in healthcare settings since 2006; 2) Identify the pathogen reservoirs and forms of transmission;

3) Describe the antimicrobial resistance profiles; 4) Identify and describe infection control practices. This systematic review followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (Page et al., 2021). Data were obtained from three databases including PubMed, EMBASE, and Web of Science. All three databases were last searched on March 17th, 2023, using key words and MeSH Terms in Table 3. Publication dates were limited from January 1, 2006, to the present. Results were also limited to the English language.

Table 3. Search Terms by Database and Number of Records

Database	Date	Search Terms	Records
PubMed	March 17, 2023	("acinetobacter baumannii"[MeSH Terms] OR ("acinetobacter"[All Fields] AND "baumannii"[All Fields]) OR "acinetobacter baumannii"[All Fields]) AND ("water"[MeSH Terms] OR "water"[All Fields] OR "watering"[All Fields] OR "water s"[All Fields] OR "watered"[All Fields] OR "waterer"[All Fields] OR "waterers"[All Fields] OR "waterings"[All Fields] OR "waters"[All Fields] OR "waterborne"[All Fields]) AND ("hospital s"[All Fields] OR "hospitalisation"[All Fields] OR "hospitalization"[MeSH Terms] OR "hospitalization"[All Fields] OR "hospitalised"[All Fields] OR "hospitalising"[All Fields] OR "hospitality"[All Fields] OR "hospitalisations"[All Fields] OR "hospitalizations"[All Fields] OR "hospitalize"[All Fields] OR "hospitalized"[All Fields] OR "hospitalizing"[All Fields] OR "hospitals"[MeSH Terms] OR "hospitals"[All Fields] OR "hospital"[All Fields]) AND ("disease outbreaks"[MeSH Terms] OR ("disease"[All Fields] AND "outbreaks"[All Fields]) OR "disease outbreaks"[All Fields] OR "outbreak"[All Fields] OR "epidemiology"[MeSH Subheading] OR "epidemiology"[All Fields] OR "outbreaks"[All Fields] OR "outbreak s"[All Fields])	43
EMBASE	March 17, 2023	acinetobacter AND baumannii AND (water OR waterborne) AND hospital AND ('outbreak'/exp OR outbreak)	27
Web of Science Core Collection	March 17, 2023	(Acinetobacter baumannii) AND (water OR waterborne) AND (hospital) AND (outbreak)	61

2.2 Inclusion and Exclusion Criteria

The following criteria were required for inclusion: 1) A primary study on an *A. baumannii* outbreak in the hospital setting; 2) Outbreaks since 2006. Studies that were not available in English, focused on pathogens other than *A. baumannii*, were not in the hospital setting, or were unavailable as full text were excluded.

2.3 Screening and Data Extraction

The author screened reports as a single reviewer. After the databases were searched using key terms, reports were filtered by date and language. After filtering, all retrieved reports were saved to Zotero. Duplicates were manually removed. Titles and abstracts were screened by the reviewer. Some were excluded for irrelevance, and the remaining reports were considered for full review. Of those retrieved, the author further assessed eligibility based on the inclusion criteria. The data elements extracted from the final reports included: 1) Author/year; 2) Country; 3) Type of Study; 4) Setting; 5) Reservoirs; 6) Antimicrobial Susceptibility; 7) Results and Infection Control.

3. RESULTS

3.1 Included Studies

A total of seven studies were included for final review (Table 4). A total of 131 articles were identified from PubMed (n=43), EMBASE (n=27), and Web of Science (n=61). An additional 59 articles were removed by filtering for publication date and the English language (n=32) or removed as duplicates (n=27). Of the remaining 72 articles to be screened, 17 were excluded due to irrelevant titles or abstracts. Next, 55 articles were sought for retrieval, while nine could not be retrieved due to lack of full text availability. Finally, 46 articles were reviewed further for eligibility. Of those excluded, ten were excluded as non-primary articles, nine articles did not focus on the pathogen of interest, eighteen were outside of scope or non-outbreak focused, and two articles involved outbreaks prior to 2006.

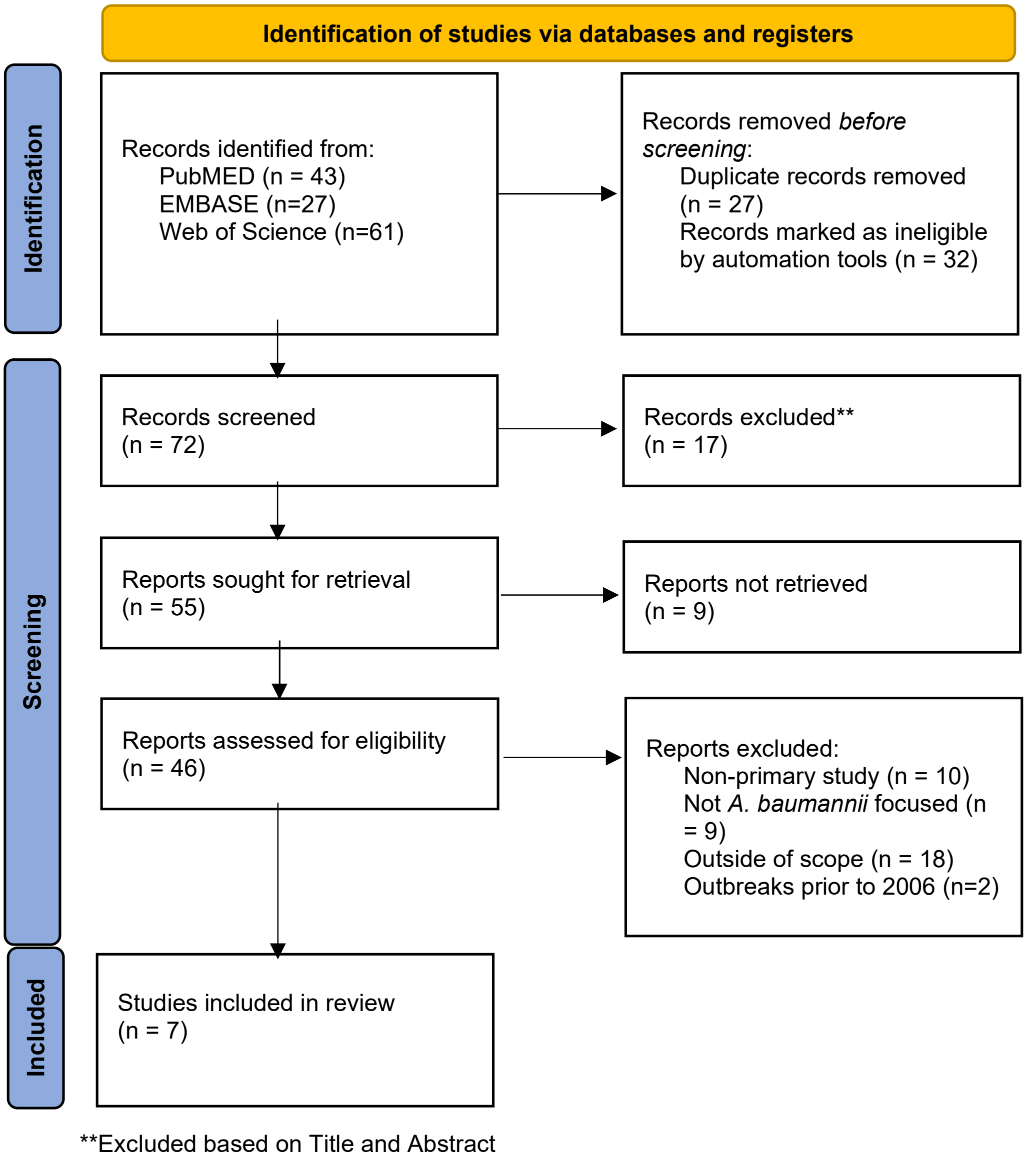

Figure 2. PRISMA Flow Diagram of Literature Review

Table 4. Summary of Final Studies

Author/Year	Country	Type of Study	Setting	Sample Size (N=)	Reservoirs	Antimicrobial Susceptibility	Infection Control	Outcomes Measured
Byun et al., 2021	Republic of Korea	Retrospective Case Control Study (N=427)	Pediatric Intensive Care Unit	427 patients	Computer keyboard and condensed water in ventilator circuits	Colistin, Minocycline, Tigecycline, and Amoxicillin/Sulbactam	Cohort isolation, hand hygiene promotion, universal contact precautions, and environment management, surveillance, and monitoring and feedback	29 out of 427 patients confirmed to have MDRAB colonization
Lee et al., 2022	Hong Kong	Descriptive Study	Acute Care Hospital with medical surgical specialties, both inpatient and outpatient	17 environmental samples, 58 patients	Laundry evaporative cooler and the laundry environment	Ceftazidime	New laundry cart system, increased environmental cleaning, decreased central laundry burden, replaced contaminated evaporative coolers	58 patients infected or colonized; 4 of 17 sampled sites were positive for A. *baumannii*
Lv et al., 2019	People's Republic of China	Matched Case-Control Study	Neurosurgical Intensive Care Unit	6 cases and 12 controls	Faucet aerator	Tigecycline	Hand hygiene compliance, isolation and cohorting, fluorescent labelling, aerosolized hydrogen peroxide for terminal cleaning, universal contact precautions, retraining of staff	Cases and controls did not differ significantly for studied characteristics; Faucet aerator strain matched clinical isolates
Cristina et al., 2013	Italy	Descriptive, Retrospective Study	Multiple Wards: ICU, general surgery, geriatrics, sub-ICU, internal medicine, and gastroenterology	Patients: 102 in ICU, 158 in sub-ICU, 872 in general surgery, 302 in geriatrics, 485 in internal medicine, 404 in gastroenterology; 131 environmental samples	No common source implicated	Not reported	Isolation, cohorts, periodic meetings of staff, hand hygiene checks, stricter controls of behavioral protocols, obligatory placement of medical devices and personal protective equipment, sanitation operations	22 patients involved in outbreak; *A. baumannii* was not isolated from environmental samples
Umezawa et al., 2015	Japan	Descriptive Study	Emergency Intensive Care Unit	18 patients; Number of environmental samples not reported	Contaminated tap water	Not reported	Replacement of contaminated portions of water system, daily cleaning of water taps and oral care with dry method	3 patients under mechanical ventilation with pneumonia and 15 patients under tracheal ventilation receiving wet oral care without pneumonia
Landelle et al., 2013	France	Descriptive Study	5 Intensive Care Units, 1 Medical Ward, 2 Surgical Wards	313 environmental samples, 86 patients	Patient carriers, contaminated environmental surfaces, contaminated healthcare worker hands	Colistin	Cohorting in a dedicated isolation unit, contact precautions, environmental screening, HCW auditing, hydrogen peroxide mist disinfection	86 patients; 29 environmental samples positive for *A. baumannii*
Dickstein et al., 2021	Israel	Quasi-experimental, Retrospective Study	Neurosurgical Intensive Care Unit and Inpatient Hematology Department	122 patients	Sustained environmental contamination	Not reported	Wall painting following chlorine disinfection after patient discharge	92% decrease in Carbapenem resistant *A. baumannii* following intervention

3.2 Reservoirs

A total of six studies included environmental sampling as a part of their epidemiologic investigations of *A. baumannii* outbreaks within hospital settings. Only one study was unable to implicate an environmental reservoir in its outbreak investigation, as environmental sampling produced negative results for *A. baumanni*. However, the study concluded that transmission most likely occurred from intra-hospital movement of the index patient with cross-contamination from healthcare workers (Cristina et al., 2013). Out of the six studies who performed environmental sampling, four investigations identified water sources as reservoirs for *A. baumannii* within their facilities. These reservoirs included condensed water in ventilator circuits presumed to be contaminated by healthcare workers or respiratory droplets of colonized patients, faucet aerators, colonization in water system via sink taps of an Emergency Intensive Care Unit, and the evaporative cooler in the laundry facility at a hospital (Byun et al., 2021; Landelle et al., 2013; Lee et al., 2022; Lv et al., 2019; Umezawa et al., 2015). Of note, the facility investigating the faucet aerators was unable to determine if contamination was caused by other water related sources such as the pipeline or municipal water versus contaminated healthcare worker hands (Lv et al., 2019). Otherwise, three investigations implicated dry environmental surfaces such as keyboards, laundry racks, monitors, cooling blankets, computers, and patient washing basins (Byun et al., 2021; Landelle et al., 2013; Lee et al., 2022). Landelle et al. also isolated *A. baumannii* in air samples (2013).

3.3 Antimicrobial Resistance

All seven studies reported outbreaks of what they classified as either carbapenem resistant, drug-resistant, or multidrug-resistant strains of *A. baumannii*. Of the seven studies, three studies did not report to which antibiotics the strains were susceptible. Only two outbreak strains were noted to be susceptible to colistin. These included a strain from a French hospital only susceptible to colistin, along with a strain from the Republic of Korea with multiple susceptibilities, including colistin, minocycline, tigecycline, and amoxicillin/sulbactam (Byun et al., 2021; Landelle et al., 2013). The Korean hospital indicated treatments were effective with these antibiotics alone or in combination (Landelle et al., 2013). In addition to the hospital in the Republic of Korea, another hospital in the People's Republic of China noted their outbreak strain was also susceptible to tigecycline (Lv et al., 2019). Otherwise, one outbreak strain in Hong Kong was only susceptible to ceftazidime. While not all studies reported susceptibility testing, those who did never indicated the identified susceptible antibiotics were ineffective. This supports the need for susceptibility testing as a means for determining treatment in the presence of resistant strains, especially in outbreak settings.

3.4 Infection Control Practices

All seven outbreak responses included different forms of improved or enhanced infection control practices. Infection control practices are summarized in Table 5. The practices included in the table refer to infection control interventions that were identified as contributing to the end of *A. baumannii* transmission within the facility and subsequently, the end of the outbreaks.

Table 5. Infection Control in Outbreak Response

Infection Control Intervention	**Number of Facilities (n=7)**	**Prevalence**
Enhanced Hand Hygiene*	4	57%
Isolation/Cohorts	4	57%
Contact Precautions	2	29%
Enhanced Environmental Cleaning**	7	100%

Wall Painting with Acrylic Paint Following Discharge	1	14%
Enhanced Surveillance	1	14%
Equipment Replacement***	2	29%
Staff Re-education	1	14%
Practice Change****	1	14%

*Hand Hygiene enhanced through promotion, audits, and/or compliance monitoring

**Enhanced Environmental Cleaning includes but is not limited to increased frequency of cleaning, checks with fluorescent labelling, aerosolized hydrogen peroxide, and chlorine disinfection

***Equipment Replacement includes replacing contaminated faucet aerators, contaminated hand hygiene sinks, and contaminated evaporative laundry cooler

****Practice Change refers to switching from wet oral care to dry oral care due to potentially contaminated water sources

4. DISCUSSION AND CONCLUSION

4.1 Discussion of Research Questions

This review examined global literature on water-related outbreaks caused by *A. baumannii* in healthcare settings after the year 2006. The main areas of focus included the reservoirs, antimicrobial susceptibility, and infection control practices of the outbreaks. Examining these aspects of current outbreaks is vital to understanding how to reduce transmission in similar settings in the future. While methods of detection are important for timely identification of clusters and outbreaks, the topic was excluded from the final analysis due to inconsistent reporting and explanation of methods between studies. Every outbreak examined in this review involved a drug resistant strain of *A. baumannii*. This further supports CDC's classification of *A. baumannii* as an urgent threat and corroborates the growing concern for the impacts of antimicrobial resistant pathogens. Furthermore, *A. baumannii* was found in a multitude of reservoirs within the hospitals, which affirms its ability to persist in different environments. However, while portions of the facilities' water systems may have been contaminated, they were not often implicated as the main source of *A. baumanni* and were most likely contaminated via cross contamination from healthcare workers. These findings indicate that outbreaks of *A. baumannii* caused by water-related reservoirs may be rare compared to other environmental sources. Enhanced or improved infection control practices were implemented at every institution during their outbreaks, demonstrating the importance of infection control interventions in outbreak settings.

Understanding the reservoirs of *A. baumannii* within hospitals will direct prevention and control efforts, such as disinfection and cleaning. Encouragement of environmental sampling will assist with continued identification of reservoirs in the hospital setting. By increasing awareness around possible reservoirs, other facilities may take these into consideration for sampling. For example, only Landelle et al. (2013) mentioned ambient air sampling during their outbreak. Of which, some samples were positive. However, the authors also alluded to previous outbreaks finding positive ambient air samples, so this could be a neglected source of transmission being examined in outbreak responses (Landelle et al., 2013).

The lack of confirmed water-related transmission or primary source of the outbreak was an interesting finding in this review. Previous studies have identified *Acinetobacter species* in premise plumbing and hot water systems in hospitals (Baron et al., 2014; Cristina et al., 2014). Furthermore, the ability to create biofilms is thought to contribute to species', such as *Acinetobacter*, ability to persist in premise plumbing (Cristina et al., 2014). However, not all studies performed environmental sampling to investigate water sources as a reservoir. Additionally, this aligns with Kizny et al. suggesting that the healthcare water environment may be neglected during outbreak assessments (Kizny Gordon et al., 2017).

All seven studies in this review reported investigating resistant strains of *A. baumannii*, four of which noted resistance to carbapenems (Byun et al., 2021; Dickstein et al., 2021; A. L. H. Lee et al., 2022; Lv et al., 2019) . This is especially concerning because carbapenem resistance driven by *A. baumannii* production of carbapenemases can spread to other pathogens, thus increasing the issue of effective treatments for a multitude of infections (CDC, 2019). Out of the seven studies, only four investigations reported antimicrobial susceptibility on their outbreak strains. Only one study reported susceptibility to ampicillin/sulbactam, which is currently the IDSA's first drug of choice (Tamma et al., 2022). Therefore, examining the antimicrobial resistant profiles is increasingly important considering the CDC and WHO's priority concerns around *A. baumannii*. Reviewing studies focused solely on antimicrobial resistance of *A. baumannii* was outside the scope of this study. However, recognizing the disparity between methods, antibiotics included in susceptibility testing, along with reporting of results from outbreak investigations highlights the need for transparency to better understand the characteristics of this priority pathogen.

Infection control practices were reported for all seven outbreaks. However, it is important to note that the direct effect of each practice is difficult to assess. For example, while hand hygiene was mentioned in four studies, some reports indicated that healthcare workers' hands were not sampled, so transmission by healthcare workers could only be speculated (Cristina et al., 2013; Landelle et al., 2013). Additionally, environmental cleaning was mentioned in all outbreaks yet was not always expanded upon. While studies focused solely on *A. baumannii* susceptibility to different disinfectants and cleaners were beyond the scope of this review, understanding what products may have contributed to reduced transmission in a practice setting would be helpful for future responses.

4.2 Limitations

Several limitations exist for this study. A single reviewer performed the systematic review possibly subjecting the selection process to selection bias. The review was limited to three databases (EMBASE, PubMED, and Web of Science), so expanding to additional databases may be beneficial. Additionally, some studies were unable to be retrieved due to full text availability and time constraints. While many of the studies occurred in countries outside the United States, the selection process was limited to those available in English. Additionally, the definition for an outbreak of *A. baumannii* is not standardized globally. Therefore, some studies on *A. baumannii* clusters or investigations may have been missed during the review process if they were not flagged based on key terms for outbreaks. Similarly, surveillance for *A. baumannii* can differ dramatically across settings. Some facilities may include *A. baumannii* in routine surveillance, while others only perform screenings in the setting of an outbreak if at all.

4.3 Conclusion

This systematic review highlights the multidisciplinary approach needed to respond to outbreaks of *A. baumannii*. *A. baumanii* is frequently found in the hospital environment in a variety of niches, including on surfaces and in water, where it is persistent and difficult to disinfect. The results from this review support the need to better understand how hospital water systems, sinks, and equipment use water as a reservoir for *A. baumannii* and how best to respond to outbreaks in terms of identification, treatment, and reduction of transmission. As a priority pathogen for the CDC and the WHO, global best practices are needed to prevent outbreaks and provide effective treatment. Antimicrobial resistance is a growing concern with no indication of slowing down. Public health and healthcare recommendations need to be based on the most current evidence available.

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Appendix A

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	i
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	i
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	1-2
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	2
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	10
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	9
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	9-10
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	10
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	10
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	10-12
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	10-12
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	17-18
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	10, 12
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	10-12
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	10-11
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	11
Study characteristics	17	Cite each included study and present its characteristics.	12
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis	

Section and Topic	Item #	Checklist item	Location where item is reported
		assessed.	
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	15-17
	23b	Discuss any limitations of the evidence included in the review.	15-18
	23c	Discuss any limitations of the review processes used.	17-18
	23d	Discuss implications of the results for practice, policy, and future research.	15-18
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	
Competing interests	26	Declare any competing interests of review authors.	
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

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