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Duration of Carriage of Multidrug-Resistant *Acinetobacter baumannii* and its Impact on Infection Control Measures and Antimicrobial Use

Summary of the Doctoral Thesis for obtaining the scientific degree "Doctor of Science (*PhD*)"

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Abbreviations used in the Thesis

A. baumannii	*Acinetobacter baumannii*
CDC	Center for Disease Control and Prevention
DNS	Deoxyribonucleic acid
ECDC	European Centre for Disease Prevention and Control
EUCAST	European Committee on Antimicrobial Susceptibility Testing
I	intermediate
MDR	multidrug-resistant
MIC	minimal inhibitory concentration
PEG	percutaneous endoscopic gastrostomy
WHO	World Health Organization
R	resistant
RAKUS	Riga East University Hospital (*latv. Rīgas Austrumu klīniskā universitātes slimnīca*)
S	sensitive
SPKC	Centre for Disease Prevention and Control of Latvia (*latv. Slimību profilakses un kontroles centrs*)
spp.	species
ST	sequence type
VAC	vacuum-assisted closure
WHO	World Health Organization

Terms

Antibacterial agent	A natural or synthetic substance that kills or inhibits the growth of bacteria
Antibacterial resistance	Bacterial insensitivity to antimicrobial agents
Antimicrobial agent	A natural or synthetic substance that kills or inhibits the growth of various microorganisms (e.g. bacteria, fungi, viruses, etc.)
Antimicrobial resistance	Insensitivity of microorganisms to antimicrobial agents
Healthcare-associated infections	Infections that people get when they receive healthcare for another medical condition
Bloodstream infection	Bacteraemias or septicaemias – serious health conditions when bacteria or other microorganisms enter the blood, causing an infection
Biofilm	A complex collection of micro-organisms that attach to surfaces and form a structured community surrounded and protected by a self-produced extracellular polymeric material, which can grow in both natural and artificial environments
Isolate	A single isolate of a single bacterial species
Colonisation	Occurs when microorganisms are present on an individual who has no clinical symptoms or signs of active disease.
Contamination	Contamination with microflora of material collected by non-aseptic technique for microbiological testing
Resistance	Insensitivity
Selective pressure	A result of antimicrobial use in which bacteria initially susceptible to antimicrobials are killed by the antimicrobial, allowing bacteria resistant to the antimicrobial to survive and multiply

Introduction

Riga East University Hospital is the largest multi-profile healthcare institution in Latvia, providing comprehensive diagnostics and treatment for patients, as well as conducting scientific research, developing innovations, training new specialists and implementing public education and health promotion activities. The hospital provides services in profiles that are not available in other Latvian inpatient healthcare institutions, such as microsurgery, plastic and reconstructive surgery, treatment of *decubitus*, toxicology, sepsis, polytrauma profile, treatment of burns and frostbite, paediatric surdology, stem cell transplantation, treatment of tuberculosis, HIV/AIDS and stereotactic radiotherapy for oncology patients. In 2023, the hospital provided healthcare services to approximately 55 000 inpatients and 840 000 outpatients, with a total of more than 2 000 beds throughout the hospital. During 2023, more than 72 000 different types of operations were performed and the hospital employed almost 5 000 staff.

The epidemiological situation of *A. baumannii* in Europe has worsened in recent years. The number of countries reporting interregional spread of resistant *A. baumannii* has increased rapidly. Between 2017 and 2021, the average percentage of countries in the European Union / European Economic Area with combined resistance to carbapenems, fluoroquinolones and aminoglycosides increased significantly from 32.1 % to 36.8 % (ECDC, WHO. 2023).

The latest available data on *Acinetobacter* resistance in Latvia show an increasing trend (ECDC, 2024). In 2022, Latvia still has one of the highest resistance rates of *A. baumannii*: 63.3 % of *Acinetobacter spp.* isolates have the combined resistance to fluoroquinolones, aminoglycosides, carbapenems. Compared to other European countries, a much better situation can be noted, e.g. Ireland, Norway and Belgium, where in 2022 there were no *Acinetobacter* with such resistance, and a relatively better situation, e.g. Sweden 1.4 %, Portugal 19.3 %.

Antimicrobial resistance is a major problem in Latvian hospitals. *A. baumannii* resistance affects the aetiology of healthcare associated infections, infection control and choice of antibacterial treatment. To improve the current situation, antimicrobial stewardship programmes should be more rigorously and widely implemented to promote more appropriate antimicrobial use and reduce the problem of antimicrobial resistance (WHO Regional Office for Europe, 2021). The implementation of these prevention measures in hospitals would reduce the number of resistant *A. baumannii* cases, including by focusing on the correct choice of drugs to reduce selection pressure and further spread of resistant strains (Owens et al., 2006; Perez et al., 2007; ECDC, 2016(2); ECDC, WHO. 2023).

In his 2014 review on antimicrobial resistance, British economist Jim O'Neill predicted that, without strong countermeasures, 10 million people a year worldwide could die from infections with resistant microorganisms by 2050, more than currently die from cancer. In 2014, 700 000 deaths were linked to resistance worldwide. This review also states that costs will rise to £63 trillion (O'Neill, 2014). Meanwhile, a more recent WHO report states that the World Bank estimates that up to 3.8 % of global gross domestic product could be lost to antimicrobial resistance by 2050 (WHO, 2022). Both the WHO review and the Jim O'Neill report mention that joint replacement, caesarean section, chemotherapy and various types of transplantation are among the many treatments that depend on available antimicrobials to prevent infections. Without effective antimicrobials, these treatments would become riskier and, in many cases, impossible.

The looming crisis can be averted by changing antimicrobial use patterns, the development of new antimicrobials and the need for concerted international action on antimicrobial use in humans and animals.

The most common healthcare-associated infections are caused by a group of micro-organisms called "ESKAPE" pathogens. This group includes

Enterococcus faecium, *Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa* and *Enterobacteriaceae* because they often develop resistance to antibacterial agents.

In 2017, the WHO published a list of "priority" microorganisms against which work on new antimicrobials is urgently needed. One of the bacteria that has been given a first, or critical, priority is resistant *Acinetobacter baumannii* (WHO, 2017). The latest version of this list keeps carbapenem-resistant *Acinetobacter baumannii* on the critical priority list (WHO, 2024).

Riga East University Hospital (RAKUS) is one of the largest and most prestigious medical institutions in Latvia. It is accredited as a clinical university hospital, which means that it is closely linked to the process of medical education and research. The hospital provides a wide range of clinical services, including outpatient treatment, inpatient care, diagnostic procedures and surgical interventions. RAKUS is often at the forefront of medical education and research and is a place where specialised care is provided for a wide range of diseases. As an important healthcare institution in Riga and Latvia, RAKUS plays an important role in both patient care and the development of medical science in the country. However, RAKUS has shown an increasing trend in recent years in terms of hospital-acquired infections with resistant *Acinetobacter baumannii*.

A. baumannii can be present in the human body without causing an infectious process. However, it is dangerous because it can spread and cause infection in patients who are already ill or have a reduced immune response, especially in intensive care unit patients and those suffering from comorbidities. Intensive care patients are often very vulnerable to infections and may have a reduced immune response due to severe trauma, surgery or chronic diseases. In addition, patients with comorbidities such as diabetes or chronic lung disease may be more susceptible to any type of infection, including infections caused by

A. baumannii (Kucukler, 2014; Ren et al., 2019; Dezza et al., 2023; Benaissa et al., 2023).

It is therefore extremely important to follow infection control measures in intensive care units and other wards where these patients are treated. These measures include essential elements such as strict hand hygiene and knowledge and monitoring of the rational use of antimicrobials. This is aimed at reducing the spread of *A. baumannii* and its potential impact on hospital patients and antimicrobial resistance in general.

The most common sites of *A. baumannii* colonisation are the throat, respiratory tract, perineum (Seifert et al., 1997), while the most common infections associated with resistant *A. baumannii* are central vascular catheter-associated sepsis, central nervous system infection, surgical wound infection and pneumonia (Dexter et al., 2015).

Patients colonised with resistant microorganisms, including re-admissions to hospital, are a potential source of infection and subject to subsequent infection control, and pose a challenge to clinicians in their daily practice when empirical antimicrobial treatment of severe infections or antimicrobial prophylaxis is required.

Currently, there is little information on how long *A. baumannii* colonises humans after infection and therefore it is not possible to say with certainty whether patients with a history of resistant *A. baumannii* require infection control measures in the event of readmission and whether empirical antimicrobial therapy or prophylaxis against resistant *A. baumannii* should be used if necessary.

Aim of the Thesis

The aim of this study is to investigate the duration of carriage of resistant *A. baumannii* after infection.

Tasks of the Thesis

To achieve the aim of the Doctoral Thesis, the following tasks have been set:

1 To determine the duration of carriage of resistant *A. baumannii* during the study period.
2 To determine the risk factors for carriage of resistant *A. baumannii*.
3 To clarify the syndromes and diseases of infection caused by resistant *A. baumannii*.
4 To clarify the risk factors for infection with resistant *A. baumannii*.
5 To clarify the relationship between colonisation by resistant *A. baumannii* and infectious manifestations.
6 Identify anatomical sites of colonisation of resistant *A. baumannii* in the body.
7 Perform whole genome sequencing of resistant *A. baumannii* to prove the identity of *A. baumannii* in case of re-isolation during dynamic surveillance.

Hypotheses of the Thesis

1 **Hypothesis 1:** Resistant *A. baumannii* is a colonising microorganism in most patients, but is potentially dangerous in intensive care unit patients and patients with comorbidities.
2 **Hypothesis 2:** The rate of disappearance of resistant *A. baumannii* from the resident human microflora is uncertain.

Novelty of the Thesis

In Latvia, no studies have yet been conducted on the duration of carriage of resistant *A. baumannii* after infection and its impact on infection control and antimicrobial use. Such studies are useful to understand the nature of the spread of this pathogen and to develop effective control measures.

It is important to focus attention on this type of research and its potential impact on practice in the Latvian scientific community and healthcare institutions. In the face of conflicting assessments and data on such studies, it would be worth further discussion and research to assess their real potential and benefits in the Latvian healthcare context.

The aim of this work is very important, especially given the complex nature of *A. baumannii* infections and their prevalence in healthcare settings. The aim of this study, to determine the duration of carriage of resistant *A. baumannii* after infection, may contribute significantly to the development and improvement of generally accepted infection control strategies and to the rational use and effectiveness of antimicrobial agents.

The results of the study may provide information on the duration of *A. baumannii* persistence after infection, which is an important factor in determining the optimal time frame for preventing and controlling the spread of infection. In addition, it may provide suggestions on the duration and type of antimicrobial treatment to effectively combat the pathogen, minimise the development of resistance and reduce the spread of infections.

Finally, the results of the study could provide a basis for further development of strategies and adoption of measures to improve infection control and reduce the burden of *A. baumannii* infections in healthcare settings.

1 Materials and methods

1.1 Design

The scientific work is a longitudinal analytical study of a cohort of patients. The study included patients treated at Riga East University Hospital from 1 November 2015 to 30 June 2016 who were isolated with multidrug-resistant *A. baumannii*. Subsequently, these patients were followed up as outpatients until 2018. A patient questionnaire was completed for each patient (Annex 1). The following general data were collected for all included patients: sex; age; date of initial hospitalisation; place of hospitalisation; initial diagnosis; comorbidities; medical history; hospital risk factors and outcome of the initial hospitalisation. Data on antimicrobial use prior to *A. baumannii* diagnosis were collected. For identified *A. baumannii*, the date of initial isolation, antimicrobial susceptibility and site of initial isolation or localisation were collected. *A. baumannii* colonisation or infection was subsequently defined according to the ECDC case definition of healthcare associated infection (ECDC; 2016(1)). Patients discharged from hospital were dynamically followed up as outpatients at months 1, 3, 6, 12 and 18, with *A. baumannii* swabs taken at each visit (see Figure 1.1).

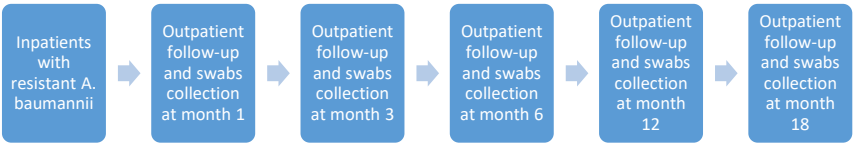

Figure 1.1 **Design scheme**

1.2 Methods

A. baumannii isolates were obtained from patient samples during microbiological analysis, selectively cultured on *MacConkey* agar (*HiMedia,* India) according to the laboratory methodology. Culture identification and phenotypic antimicrobial susceptibility were performed using *VITEK®2 GN* identification and *VITEK® AST* broth microdilution cards (*bioMerieux,* France). Antibacterial susceptibility interpretation was performed according to the EUCAST current rules 2015–2018 (version 5.0, valid from 01.01.2015–31.12.2015; version 6.0, valid from 01.01.2016–31.12.2016; version 7.1, valid from 01.01.2017–31.12.2017; version 8.0, valid from 01.01.2018–16.05.2018; version 8. 1, valid 16.05.2018–12.18.2018 (EUCAST, 2024)) using the *VITEK® AST* microdilution card readings for the following antimicrobials: ciprofloxacin, piperacillin/tazobactam, ampicillin/sulbactam, ceftazidime, imipenem, meropenem, gentamicin, amikacin and colistin. According to the MIC obtained, isolates from patients included in the study were classified as sensitive, moderately sensitive, or resistant. These terms were used in the work without taking into account the revision of the sensitivity definitions in 2019 and their implementation in practice from 2020, where the interpretation of antimicrobial sensitivity is defined as sensitive at standard dose, sensitive at increased dose and resistant (version 10.0, valid from 01.01.2020–31.12.2020) (EUCAST, 2021).

In 2011, a joint initiative of the European Centres for Disease Control and Prevention (ECDC) and the Centers for Disease Control and Prevention (CDC, USA) in Europe and the United States proposed specific definitions to describe antimicrobial resistance in microorganisms that cause many healthcare associated infections (Magiorakos et al, 2011), however, both before and after this publication, the term “multidrug-resistant” is widely used, which partly explains the considerable heterogeneity of clinical studies assessing the different

antimicrobial resistance data in *Acinetobacter* infections. Therefore, for simplicity, *A. baumannii* that have retained antimicrobial susceptibility to amikacin and colistin or to colistin alone are included in the study. Both of these groups are considered epidemiologically important from an infection control point of view, clearly have reduced antimicrobial susceptibility, require strict infection control measures and can be defined as resistant microorganisms.

During the dynamic observation, samples for microbiological examination were obtained by the "sponge" method. A sterile viscose sponge (*Copan Italia S.p.A, Italy*) moistened in saline was used to wash an area of skin approximately 15 × 15 cm^2 by gently rotating it, followed by placing the sponge in 50 ml trypticase soy broth (*Tryptone Soy Broth, HiMedia Laboratories,* India) and incubating for 20–24 h at 37 °C for bacterial multiplication. After 18–20 h of incubation, the broth was homogenised in a barrel and 100 µl of its contents were transferred to a selective MacConkey agar (*MacConkey Agar, HiMedia Laboratories,* India) plate. In addition to the selection of resistant strains of Gram-negative bacteria, an aztreonam disc (*Aztreonam 30 µg, Liofilchem S.r.l.,* Italy) was placed on each plated plate. The plates were incubated at 37 °C. After incubation for 20 to 24 h, the grown colonies were examined. Pale, lactose-fermenting, oxidase-negative colonies morphologically matching *A. baumannii* were further identified by the *Vitek2* system (*Vitek®2 GN, bioMeriuex,* France).

Whole genome sequencing (WGS) was used to identify *A. baumannii* isolated during primary hospitalisation and during dynamic surveillance as identical. The isolates were cultured on nutrient agar (*Biolife, Italy*) at 37 °C for 24 hours. For genomic DNA extraction, an isolate from each single colony was selected, resuspended in 180 µl lysis buffer from the *QIAamp DNA Mini* Kit (*QIAGEN Manchester Ltd.* Manchester, UK) and treated according to the manufacturer's protocol for gram-negative bacteria. DNA concentrations

were measured on a Qubit and used to construct 1 ng using a Nextera XT preparation kit (*Illumina,* San Diego, USA). Sequencing was performed at the BIOR Institute for Food Safety, Animal Health and the Environment with Illumina Miseq using V3 chemistry for 2×300 *bp* final reads. *Velvet 1.1.04* was used for genome assembly, each sequence was trimmed to an average *Phred* quality of 30 from a 20 *bp* window and *de novo* genome assembly was performed. The estimated genome size was 3.9 Mb and the target coverage was 70-fold. Genome assembly was assessed by N50 (minimum 10 000) and average genome coverage (minimum 30-fold). The genetic relatedness of the *A. baumannii* genomes was analysed using Ridom SeqSphere+ 5.0.0 software (*Ridom,* Germany). Genome comparisons were performed based on the multilocus sequence typing (MLST) scheme developed at the Pasteur Institute and nuclear genome (cg) MLST.

1.3 Statistical methods

Common descriptive statistical methods were used to characterise patient parameters. The correlation between patient characteristics was analysed using factor coding. The correlation between parameters was assessed using statistical tests: 2x2 table, χ^2 test (in case of insufficient sample size, Fisher's exact test was used) and t-test. For a more in-depth study of the data, a logistic regression analysis was performed, which was used to create predictive models. The model parameters are calculated in the statistical package SPSS using a method that estimates the effect of all independent variables in aggregate. The statistical significance of each parameter was assessed using the *Wald* test. A parameter was considered significant if the p-value associated with the test was less than or equal to 0.05. The fit of the logistic regression model to the overall dataset is assessed using the *Omnibus* test and the *Hosmer-Lemeshow* test to assess that the resulting model is adequate for the experimental data. A model is considered adequate if the p-value associated with the test is less than or equal to 0.05.

Classification into predicted outcomes was performed by comparing the P(Y) calculated within the model with a selected threshold value. ROC-curves were used to compare the predictive ability of the different models. ROC curves were obtained by varying Pr and plotting the proportion of correctly classified cases with outcome Y against the proportion of misclassified cases without outcome Y (false positive rate, FPR).

2 Results

2.1 Characteristics of the observation group

From 1 November 2015 to 30 June 2016, 90 patients were treated for multidrug-resistant *A. baumannii* at Riga East University Hospital, 56 patients were discharged and the remaining 34 patients died. *A. baumannii* infection was observed in 30 of the 90 patients (33 %), the presence of *A. baumannii* was determined as colonisation in the rest. The types of infections among patients were distributed as follows (see table 2.1):

Table 2.1

Types of *A. baumannii* infections

Type	Number of patients	(%)
Bone-joint infection	1	3
Bloodstream infection	6	20
Central nervous system infection	1	3
Respiratory tract infection	15	50
Surgical wound infection	5	17
Urinary tract infection	2	7
Total	30	100

The lethal outcome was 38 % in patients with *A. baumannii* infection or colonisation.

The study included 30 females (33 %) and 60 males (67 %). The mean age was 60 ± 17 years. The swab in which *A. baumannii* was identified was taken on average on day 12 ± 6.0 of hospital admission for clinical indications.

Because of the severe initial condition, 61 of 90 (68 %) patients were admitted to intensive care with the following initial reasons for hospitalisation (see Table 2.2).

Table 2.2

Reasons for intensive care hospitalisation

Reason	Number of patients	(%)
Sepsis / severe bacterial infection	19	31
Trauma/polytrauma	16	26
Stroke / cerebral haemorrhage	14	23
Other	12	20
Total	61	100

In 19 % of patients identified with *A. baumannii*, at least one of the following risk factors was identified before hospitalisation (see Table 2.3).

Table 2.3

History of risk factors

Risk factors	Number of patients	(%)
Previous hospitalisation (within the last year)	10	11
Outpatient visit (in the last year)	1	1
Both hospitalisation and outpatient visit	6	7
Clients of a social care institution	3	3
Total	17	19

16 % of the patients in whom *A. baumannii* was identified had chronic wounds.

33 % of patients identified with *A. baumannii* had one or more comorbidities (see Table 2.4).

Table 2.4

Comorbidities

Comorbidity	Number of patients	(%)
Chronic heart failure	8	9
Chronic renal failure	5	6
Diabetes mellitus	3	3
Oncological disease	3	3
Heart and kidney failure	4	4
Heart failure and diabetes	4	4
Kidney failure and diabetes mellitus	1	1
Heart, kidney failure and diabetes	1	1
Diabetes mellitus and oncological disease	1	1
Total	30	33

78 % of patients identified with *A. baumannii* had at least one hospital risk factor during hospitalisation (see Table 2.5).

Table 2.5

Incidence of hospital risk factors for *A. baumannii* infection in patients

Hospital risk factor	Count	(%)
Central line catheter	55	61
Urinary catheter	55	61
Nasogastric probe	26	29
VAC system	11	12
Artificial lung ventilation	36	40
Haemodialysis	2	2
Another invasive device (tracheostomy, nephrostomy, ventriculostomy, PEG, etc.)	23	26
Surgery during hospitalisation	31	34
Bronchoscopy	22	24

All *A. baumannii* were resistant to ciprofloxacin, piperacillin/tazobactam, ampicillin/sulbactam, ceftazidime, imipenem, meropenem and gentamicin. Of the total, *A. baumannii* susceptibility to amikacin and colistin was 18 %, while *A. baumannii* susceptibility to colistin alone was 100 %.

A. baumannii was initially isolated from one specific site in each patient (see Table 2.6).

Table 2.6

Site of *A. baumannii* isolation

Site	Count	(%)
Blood	7	8
Urine	7	8
Bronchial lavages	28	31
Wound	22	24
Cerebrospinal fluid	2	2
Other material (from bone, screening, etc.)	24	27
Total	90	100

41 % of patients received antibacterial treatment for their underlying disease before *A. baumannii* was detected (see Table 2.7).

Table 2.7

Use of antibacterials before detection of *A. baumannii*

Use of antibacterials	Count	(%)
Do not use	53	59
1 medication	12	13
2 medicines	22	24
3 medicines	2	2
Medication not known	1	1
Total	90	100

Patients were treated for their initial underlying conditions with certain classes of antibacterials before *A. baumannii* was identified (see Table 2.8).

Table 2.8

Classes of antibacterials prior to *A. baumannii* detection

Class of antibacterials	Count	(%)
3rd generation cephalosporins	12	13
Antipseudomonal fluoroquinolones	3	3
Beta-lactamase inhibitor antipseudomonal penicillin's	8	9
Carbapenems	16	18
Polymyxins	1	1
Other	22	24

After discharge from hospital, study patients were dynamically followed up on an outpatient basis over a period of 18 months. 56 patients with *A. baumannii* were discharged from hospital. Dynamic outpatient visits were scheduled at months 1, 3, 6, 12 and 18 after hospital discharge. During the visits, material was collected for the detection of *A. baumannii*. During this period, a decrease in the number of patients colonised with *A. baumannii* was observed (see Table 2.9 and Figure 2.1).

Table 2.9

Number of patients colonised with *A. baumannii* during the surveillance period

Surveillance period	Number of colonised patients	(%)
After discharge	56	100
1 month	12	21
3 months	6	11
6 months	3	5
12 months	2	4
18 months	0	0

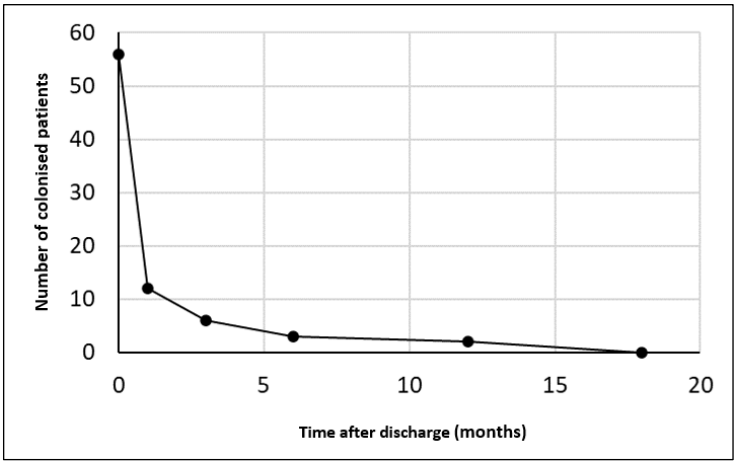

Figure 2.1 **Number of patients colonised with *A. baumannii* during the surveillance period**

2.2 Parameter correlation results

The analysis of the factors influencing the results of the study compared the results obtained in the study in order to understand which factors are relevant and which are not. The p-values of the factors were then examined to understand the significance of the influencing factors more clearly.

Relationship of lethal outcome to the predictors (see Table 2.10).

Table 2.10

Relationship of lethal outcome to descriptors

Factors	p-value*	Impact of the factor	Type of test
Infection	0.40	Not affected	2×2 table, χ^2 tests
Sex	0.32	Not applicable	2×2 table, χ^2 tests
Age	0.67	Not applicable	t-test for unpaired data
Date of detection of *A. baumannii*	0.67	Not applicable	t-test for unpaired data
Risks of medical history**	0.97	Not applicable	Table 2×2, χ^2 test
Chronic wounds	0.07	Possible	Table 2×2, Fisher's exact test
Intensive care hospitalisation	0.66	Not applicable	Table 2×2, χ^2 test
Hospital risks***: A	0.11	Not applicable	Table 2×2, χ^2 test
B	0.29	Not applicable	Table 2×2, χ^2 test
C	0.22	Not applicable	Table 2×3, χ^2 test
Comorbidities	0.03	Impact	Table 2×2, χ^2 tests
Sensitivity to amikacin	0.24	No impact	2×2 table, χ^2 tests
Antimicrobial therapy prior to detection of *A. baumannii*	0.01	Impact	2×2 table, χ^2 tests

*$p < 0,05$
**all risks combined, grouping – 0 – no risks, 1 – at least 1 risk factor
***three different groupings were considered: A - no risk factors in group 1, at least 1 risk factor in group 2; B – no more than one (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than one (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

The data showed a statistical correlation between fatal outcome and the presence of comorbidities ($p = 0.03$) and between fatal outcome and receiving antimicrobial therapy before *A. baumannii* detection ($p = 0.01$).

Association of *A. baumannii* infection with characteristics (see Table 2.11).

Table 2.11

Association of *A. baumannii* infection with characteristic factors

Factors	p-value*	Impact of the factor	Type of test
Sex	0.033	Impact	2×2 table, χ^2 tests
Age	0.266	No impact	t-test for unpaired data
Date of detection of *A. baumannii*	<0.001	Impact	t-test for unpaired data
Risks of history**	0.924	No impact	Table 2×2, χ^2 test
Chronic wounds	0.258	No impact	Table 2×2, Fisher's exact test
Intensive therapy	0.013	Impact	Table 2×2, χ^2 test
Hospital risks***: A	0.09	No impact	Table 2×2, χ^2 test
B	0.0016	Impact	Table 2×2, χ^2 test
C	< 0.001	Impact	Table 2×3, exact Fisher test
Comorbidities	0.813	No impact	Table 2×2, χ^2 test
Sensitivity to amikacin	0.626	No impact	Table 2×2, χ^2 tests
Antimicrobial therapy prior to detection of *A. baumannii*	0.019	Impact	Table 2×2, χ^2tests

*$p < 0.05$
**all risks combined, grouping – 0 – no risks, 1 – at least 1 risk factor
***three different groupings were considered: A – no risk factors in group 1, at least 1 risk factor in group 2; B – no more than one (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than one (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

Statistical correlations were found between *A. baumannii* infection and sex ($p = 0.033$), date of analysis ($p < 0.001$), intensive care treatment ($p = 0.013$), risks associated with hospital manipulation ($p < 0.001$) and the patient having received antimicrobial therapy before *A. baumannii* detection ($p = 0.01$).

Age was associated with the characteristics (see table 2.12).

Table 2.12

Association of age with characteristics

Factors	p-value*	Impact of the factor	Type of test
Day of detection of *A. baumannii*	0.144	Not affected	t-test for correlation coefficient
History risks**	0.352	Not applicable	t-test for unpaired data
Chronic wounds	0.444	Not applicable	t-test for unpaired data
Intensive care	0.793	Not applicable	t-test for unpaired data
Hospital risks*** A	0.87	Not applicable	t-test for unpaired data
B	0.54	Not applicable	t-test for unpaired data
C	0.694	Not applicable	One-factor ANOVA*
Comorbidities	0.023	Impact	t-test for unpaired data
Sensitivity to amikacin	0.102	No impact	t-test for unpaired data
Antimicrobial therapy prior to detection of *A. baumannii*	0.056	Impact	t-test for unpaired data

*$p < 0,05$
**analysis of variance (ANOVA) – t-test analogue for three or more groups
***three different groupings were considered: A – no risk factors in group 1, at least 1 risk factor in group 2; B – no more than 1 (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than 1 (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

There is a statistical correlation between age and comorbidity ($p = 0.023$).

The association of the day of hospitalisation on which the swab identifying *A. baumannii* was taken with the characteristics (see Table 2.13).

Table 2.13

Association of days of hospitalisation with *A. baumannii* identified swab with descriptive factors

Factors	p-value*	Impact of the factor	Type of test
Medical history risks**	0.154	Not affected	t-test for unpaired data
Chronic wounds	0.036	Impact	t-test for unpaired data
Intensive care	< 0.001	Impact	t-test for unpaired data
Hospital risks***: A	0.11	No impact	t-test for raw data
B	0.02	Impact	t-test for raw data
C	0.010	Impact	One-factor ANOVA*
Comorbidities	0.563	No impact	t-test for unpaired data
Sensitivity to amikacin	0.256	No impact	t-test for unpaired data
Antimicrobial therapy prior to detection of *A.baumanni*	0.202	No impact	t-test for unpaired data

*$p < 0.05$
**analysis of variance (ANOVA) – t-test analogue for three or more groups
***three different groupings were considered: A – no risk factors in group 1, at least 1 risk factor in group 2; B – no more than 1 (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than 1 (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

Statistical correlations were found between the day of hospital admission on which the swab identifying *A. baumannii* was taken and the presence of wounds ($p = 0.036$), as well as with intensive care treatment ($p < 0.001$) and risks associated with hospital manipulation ($p = 0.01$).

The association of intensive care unit (ICU) treatment with characteristics (see table 2.14).

Table 2.14

Association of ICU admission with characteristics

Factors	p-value*	Impact of the factor	Type of test
Hospital risks**: A	< 0.001	Impact	2×2 table, Fisher's exact test
B	< 0.001	Impacts	Table 2×2, Fisher's exact test
C	< 0.001	Impact	Table 2×3, Fisher's exact test
Comorbidities	0.936	No impact	Table 2×2, χ^2 test
Sensitivity to amikacin	0.002	Impact	Table 2×2, χ^2 test
Antimicrobial therapy prior to detection of *A. baumannii*	0.013	Impact	Table 2×2, χ^2 test

*$p < 0.05$
*three different groupings were considered: A – no risk factors in group 1, at least 1 risk factor in group 2; B – no more than 1 (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than 1 (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

Statistical correlations were found between ICU treatment ($p < 0.001$) and amikacin sensitivity ($p = 0.002$), and the fact that the patient was treated with antimicrobial therapy before *A. baumannii* detection ($p = 0.013$).

Relationship of the parameter “Colonisation within 1 month of discharge” to predictors (see Table 2.15).

Table 2.15

Relationship of the parameter 'Colonisation within 1 month of discharge' to predictors

Factors	p-value*	Impact of the factor	Type of test
Gender	0.744	Not affected	2×2 table, Fisher's exact test
Age	0.317	Not applicable	t-test for unpaired data
Date of detection of *A. baumannii*	0.708	Not applicable	t-test for unpaired data
Risks of history**	0.230	Not applicable	Table 2×2, Fisher's exact test
Chronic wounds	0.390	Not applicable	Table 2×2, Fisher's exact test
Intensive care	0.324	Not applicable	Table 2×2, Fisher's exact test

Table 2.15 continued

Factors	p-value*	Impact of the factor	Type of test
Hospital risks***: A	0.061	Not applicable	Table 2×2, Fisher's exact test
B	0.027	Impact	Table 2×2, Fisher's exact test
C	< 0.001	Impact	Table 2×3, Fisher's exact test
Comorbidities	1.00	No impact	Table 2×2, Fisher's exact test
Sensitivity to amikacin	0.441	No impact	Table 2×2, Fisher's exact test
Antimicrobial therapy prior to detection of *A. baumannii*	0.966	No impact	Table 2×2, χ^2test
Infection (caused by *A. baumannii*)	0.018	Impact	Table 2×2, exact Fisher test

*p < 0.05
**analysis of variance (ANOVA) – t-test analogue for three or more groups
***three different groupings were considered: A – no risk factors in group 1, at least 1 risk factor in group 2; B – no more than 1 (i.e. 0 or 1) risk factor in group 1, more than 1 (2 or more) risk factor in group 2; C – no more than 1 (i.e. 0 or 1) risk factor in group 1, 2–4 risk factors in group 2, 5–7 risk factors in group 3.

Factors influencing colonisation include infection with *A. baumannii* and "Hospital risks".

2.3 Molecular biological characterisation

For all *A. baumannii* isolates isolated from patients during primary hospitalisation and dynamic follow-up, whole genome sequencing data were obtained and sequence types (ST) were determined. The main objective of the analysis was to determine that the patient had the same *A. baumannii* during dynamic follow-up that was initially identified during primary hospitalisation.

Most of the isolates initially isolated were identified as ST2 clones, with a total of five different ST clones found (see Figure 2.2).

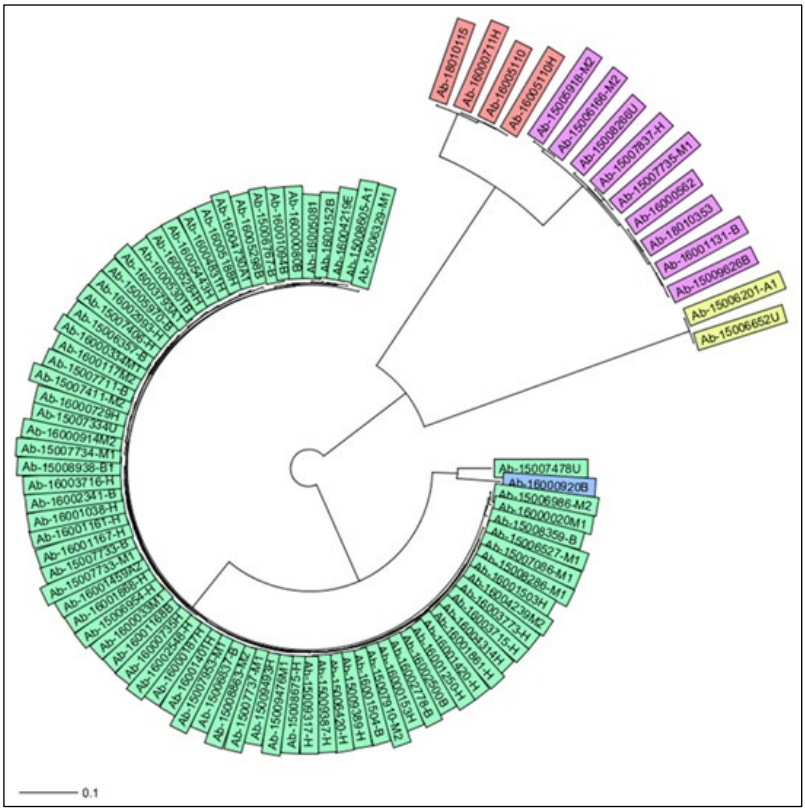

Figure 2.2 **Genetic diversity of *A. baumannii* isolates.**

ST colours: green – ST2, purple – ST286, red – ST1, yellow – ST164, blue – ST570

Analysis of the *A. baumannii* isolates isolated during dynamic surveillance showed that the isolates represented the same ST clone that was initially isolated during the primary hospitalisation (see Table 2.16).

Table 2.16

Clones of *A. baumannii* isolates during the surveillance period

***A. baumannii* isolate number at the time of primary hospitalisation**	***A. baumannii* ST clone in**				
	1st month	**3rd month**	**6th month**	**12th month**	**18th month**
Ab-16001161-H	ST2	ST2	ST2	ST2	–
Ab-16001131-B	ST286	ST286	ST286	ST286	–
Ab-15007733-B	ST2	ST2	ST2	–	–
Ab-15008359-B	ST2	ST2	ST2	–	–
Ab-16003773-H	ST2	ST2	ST2	–	–
Ab-15006837-B	ST2	ST2	–	–	–
Ab-16005188-H	ST2	ST2	–	–	–
Ab-16002341-B	ST2	ST2	–	–	–
Ab-15008675-H	ST2	ST2	–	–	–
Ab-16002500-H	ST2	ST2	–	–	–
Ab-15009493-H	ST2	ST2	–	–	–
Ab-15006767-B	ST2	–	–	–	–

In this work, 71 genes responsible for different mechanisms of *A. baumannii* pathogenesis (e.g., adherence, invasion, apoptosis induction, biofilm formation and resistance) were analysed. Each isolate contained between 53 and 71 virulence genes, but no associations were found between the *A. baumannii* virulence gene profile and other parameters such as the type of infection caused by *A. baumannii*, patient diagnosis and source of isolate. Considering the genetic diversity of *A. baumannii*, further studies are needed (Liepiņš et al., 2021).

3 Discussion

In the study, *A. baumannii* was re-identified in 21 % of cases 1 month after discharge, 11 % – in 3 months, 5 % – in 6 months and 4 % – in 12 months after discharge. At 18 months, *A. baumannii* was no longer identified in any patient. In a small Israeli study on the duration of carriage (Marchaim et al., 2007), of 30 patients identified with multidrug-resistant *A. baumannii* at least 6 months previously, repeat screening cultures were positive in 5 patients (17 %), with a median duration of 17.5 months after the last culture isolation. In contrast, 12 of 22 (55 %) patients had a positive screening culture when multidrug-resistant *A. baumannii* was isolated at least 10 days previously. It can be concluded that over a certain period, at work this was 12 months, patients after hospital discharge serve as a source of infection both in the community and in healthcare facilities in case of re-hospitalisation. The most important finding about *A. baumannii* is that the time factor is important for its disappearance.

Logistic regression statistical analysis of the effect of all parameters studied on *A. baumannii* colonisation after primary infection showed that the risk of colonisation within 1 month after discharge was higher if the patient had an *A. baumannii* infection ($p = 0.014$). The duration of colonisation was partially influenced by hospital risk factors ($p = 0.055$).

In this study, *A. baumannii* infection was confirmed in 33 % of patients, the rest were found to be colonised with *A. baumannii*. In case of colonisation, antimicrobial treatment was not necessary. It is extremely important to assess and differentiate colonisation from infection in each individual case, as this is the only way to avoid unwarranted initiation of antimicrobial therapy. In this study, 5 cases of *A. baumannii* colonisation were identified in which there were no signs of infection due to *A. baumannii*, but the patients were still treated with colistin.

In 66.6 % of patients, the presence of *A. baumannii* was defined as colonisation. Studies have observed that *A. baumannii* colonisation cases increase with increasing overall *A. baumannii* prevalence (Corbella et al., 2000; Playford et al., 2007; Arvaniti et al., 2012). It should be acknowledged that RAKUS has a long-standing endemic outbreak.

In daily practice, some doctors and researchers believe that *A. baumannii* infections are not associated with high lethality. We found that 30 % (9 out of 30) of patients with *A. baumannii* died from microbiologically confirmed *A. baumannii* infection: 6 patients with *A. baumannii* pneumonia, 2 patients with *A. baumannii* bloodstream infection and 1 patient with *A. baumannii* surgical wound infection. Healthcare professionals claim that this microorganism has not caused significantly increased mortality in hospitalised patients, so mortality due to *A. baumannii* infection remains a controversial issue (Park et al., 2013; Xiao et al., 2017). One of the analyses in this paper aimed to assess the impact of *A. baumannii* colonisation or infection on mortality. According to the literature, mortality ranges from 34 to 50 % in colonised patients and from 31 to 58 % in infected patients (Falagas et al., 2007). The heterogeneity of the studies is considered to be a factor that compromises the derivation of statistical differences between colonised and infected cases. It was not possible to tell whether *A. baumannii* infection was the direct cause of death ($p = 0.187$), but a 30 % mortality in the group of patients with *A. baumannii* infection is high. Several studies indicate that mortality associated with *A. baumannii* infection accounts for 8–43 % of total mortality (Livermore et al., 2010; Falagas et al., 2007; del Mar Tomas et al., 2005).

Mortality from septic shock due to *A. baumannii* ranges from 20–60 %, although mortality attributable to the bacteraemia itself is difficult to determine in the setting of multiple comorbidities (Seifert et al., 1995; Cisneros et al., 1996; Wisplinghoff et al., 2000; Chen et al., 2005(1); Grupper et al., 2007; Lee et al.,

2012; Brotfain et al., 2016). In the present study, fatal outcome was associated with comorbidities such as chronic heart failure, chronic renal failure, diabetes mellitus, oncological disease and various combinations of these comorbidities. In study, we observed this in 33 % of patients with 1 or more comorbidities ($p = 0.009$). The findings indicate that comorbidities are a significant risk factor for lethality when a patient is diagnosed with infection due to *A. baumannii*.

The results show that fatal outcome correlates with antimicrobial therapy before *A. baumannii* detection ($p = 0.004$). This treatment was usually associated with the main cause of hospitalisation, most commonly sepsis or another severe bacterial infection. This finding is more suggestive of *A. baumannii* as a cause of healthcare-associated infection. Also, using logistic regression statistics in the analysis of fatal outcome, it was found to be higher in patients who received antimicrobial treatment before *A. baumannii* detection ($p = 0.004$), in patients with comorbidities ($p = 0.009$), in male's ($p = 0.036$).

It is not possible to state that the patient with confirmed *A. baumannii* infection died directly from this infection, as there were additional factors that could have influenced the fatal outcome based on the initial reasons for hospitalisation: stroke, cerebral haemorrhage, severe sepsis or polytrauma. No association was found between fatal outcome and *A. baumannii* infection ($p = 0.187$).

In deceased patients compared with survivors, there were no significant differences in the frequency of hospital risk factors (presence of central line, presence of urinary catheter, presence of nasogastric probe, presence of VAC system, artificial lung ventilation, haemodialysis, surgical intervention during hospitalisation, bronchoscopy or other invasive device) ($p = 0.902$). However, higher mortality was observed in patients with comorbidities ($p = 0.009$).

Mortality due to *A. baumannii* infection is and remains a controversial issue. The analysis of mortality attributable to *A. baumannii* infection is limited

by several factors: the methodology used in the study, i.e. the spectrum of infectious causes included, and the patients' initial critical state of health.

There was a 67 % male preponderance at work. Interestingly, infection due to *A. baumannii* was more common in males ($p = 0.036$), although when comparing the effect of gender with risk factors for mortality in patients with *Acinetobacter* infection, it mentions that female gender is a risk factor (Dizbay et al., 2010), this raises more discussion and further research on the effect of gender.

Logistic regression statistical analysis showed that those patients identified with *A. baumannii* later in the day of hospitalisation ($p < 0.001$) had a higher risk of having *A. baumannii* as the causative agent of infection. This finding fully reflects the already known fact that *A. baumannii* usually causes late healthcare-associated infections (Montefour et al., 2008; Aiman El-Saed et al. 2013).

Infection due to *A. baumannii* was partially more common in patients with hospital risk factors ($p = 0.08$) but had no correlation with intensive care unit ($p = 0.239$).

Whole genome sequencing data of *A. baumannii* isolates showed that several types of ST2 clones were circulating in Riga East University Hospital during the primary data collection period of 2015–2016. The ST2 genotype is associated with multidrug resistance and was previously reported as an endemic strain in European and US hospitals, often associated with outbreaks in hospitals (Fitzpatrick et al., 2016; Liepiņš et al., 2021). In this work, sequencing was used to demonstrate that the isolate of *A. baumannii* first isolated was identical to the isolate identified by dynamic surveillance, in the same patient. Using whole-genome sequencing, it is possible to track the colonisation of a given microorganism or the progression of infection in a single patient, providing higher and more accurate surveillance of intrahospital outbreaks (Kim et al., 2018; Gramatniece et al., 2019). However, this method is expensive and

time-consuming, currently providing only retrospective data. Additionally, hospital-acquired ST2 genotypes have been found to contain specific genes, such as *bap* and *bauA*, which have been implicated in the higher prevalence of *A. baumannii* compared to other ST isolates. *Bap* is known to be involved in biofilm formation, while *bauA* is associated with iron uptake (Brossard et al., 2012; Sefid et al., 2015). The findings help to target more specific risk factors for infection and transmission of *A. baumannii* or to mitigate the impact of these factors in the hospital setting.

Infection control is of utmost importance to minimise the further spread of resistant microorganisms, including multidrug-resistant *Acinetobacter*. Identification and isolation of patients colonised with resistant *A. baumannii* is a very important measure to prevent its spread (Siegel et al., 2007).

In this study, 19 % of patients with *A. baumannii* were exposed to at least one history risk factor for *A. baumannii* infection before hospitalisation ($p = 0.715$), but the most significant of these factors was that 11 % of these patients had been hospitalised in the last year. 78 % of patients were exposed to at least one hospital-acquired risk factor for *A. baumannii* infection, but these had a partial effect on *A. baumannii* infection ($p = 0.08$). The most common hospital factors for acquiring *A. baumannii* were: central line catheter or urinary catheter, both in 61 % of cases, and 40 % of patients underwent artificial lung ventilation. In 90 % of patients not treated in the intensive care unit, the hospital risk factor score was 0 or 1 and there were no patients with more than 4 risk factors. Patients with more than 4 hospital factors were intensive care patients in 100 % of cases, with patients with more hospital factors more likely to be prescribed antimicrobial treatment. A study in South Korea (Jung et al., 2010) showed that the presence of infection and respiratory failure during ICU admission, recent central venous catheter insertion, bacteraemia caused by other microorganisms after colonisation with multidrug-resistant *A. baumannii* and

prior antimicrobial therapy were independent risk factors for bacteraemia caused by resistant *A. baumannii*. In addition, the combined factors of disinfection of the ventilator and switching from ventilator to endotracheal tube placement in the tracheostomy increased the risk of multidrug-resistant *A. baumannii* bacteraemia. Risk factors for *A. baumannii* bacteraemia in the intensive care unit have been previously demonstrated by case-control and cohort studies. Multivariate analysis of risk factors for *A. baumannii* bacteraemia showed that male sex, APACHE II score, length of ICU stays, artificial lung ventilation, previous infection, antimicrobial treatment and colonisation (Garca-Garmendia et al., 2001; Lee et al., 2004; Shih et al., 2008; Jang et al., 2009). Male gender has been cited as a risk factor in war-related work (Shih et al., 2008). In presenting work, a logistic regression statistical analysis summarising the effect of parameters on *A. baumannii* infection found that clinical infection was more common in men ($p = 0.028$).

The data showed that *A. baumannii* infection was not more common in patients treated in the intensive care unit ($p = 0.239$).

In the study, 41 % of patients received antimicrobial therapy before they were diagnosed with *A. baumannii*, and the culture in which *A. baumannii* was identified was taken on a mean of 12 ± 6.0 days of hospitalisation. This suggests that antimicrobial therapy, rightly or wrongly, prior to detection of *A. baumannii* in a patient is a partially significant risk factor for the patient becoming infected with resistant *A. baumannii* ($p = 0.082$). Logistic regression statistical analysis showed that patients who received antimicrobial treatment prior to *A. baumannii* infection have a higher risk infected with *A. baumannii* ($p = 0.039$). In this context, 31 % of patients were initially hospitalised with sepsis or other severe bacterial infection in the intensive care unit and 51 % received antimicrobial therapy before *A. baumannii* identification. Carbapenems were the most common (18 %), followed by third-generation cephalosporins (13 %) and

antipseudomonal penicillins with beta-lactamase inhibitor (9 %). One prospective study of intensive care patients concluded that there were only 2 major risk factors for multidrug-resistant infection, and these were the use of carbapenems in the last six months and the length of hospitalisation in the intensive care unit (Vasudevan et al., 2014).

In multivariate analysis, hospitalisation in the intensive care unit was one of the factors associated with infection, with the risk of infection increasing by 2 % for each additional day spent in hospital, as well as the presence of a chronic underlying condition classified as non-lethal according to the McCabe classification, which was associated with a higher risk of infection (Martin-Aspas et al., 2018). The data from the present study showed a statistical correlation between infection due to *A. baumannii* and gender ($p = 0.033$), ICU admission ($p = 0.013$), risk factors related to hospital manipulation ($p < 0.001$) and the fact that the patient was receiving antimicrobial therapy before *A. baumannii* detection ($p = 0.01$).

Pneumonia was the most frequent clinical manifestation of *Acinetobacter* infection in the study, which is consistent with other studies (Hernández-Torres et al., 2010; Munoz-Price et al., 2013; Villar et al., 2014). Mortality in the group of patients with *A. baumannii* pneumonia is high, with 40 % of patients dying, but data from several other studies are conflicting (Bouza et al., 2003; Craven et al., 2009; Dallas et al., 2011; Craven et al., 2013).

During the follow-up period, colonisation was more frequent in patients with *A. baumannii* infection and more frequent in groups exposed to hospital risk factors: in the group not exposed to risk factors or to more than one risk factor, the incidence of colonisation was 3 %, in the group with 2–4 risk factors the incidence increased to 15 %, and with 5–7 risk factors it was 23 % ($p < 0.001$).

Molecular biology analysis of *A. baumannii* isolates isolated during dynamic surveillance revealed that the isolates represented the same ST clone that was initially isolated during the primary hospitalisation.

A. baumannii colonisation 1 month after discharge is associated with *A. baumannii* infection during the initial hospitalisation and hospital risk factors.

One of the controversial issues and weaknesses of this work was that the study included cases where *A. baumannii* was not the only isolate in the primary clinical sample. In other studies, even more than 60 % of cases included the presence of polymicrobial infections (Livermore et al., 2010; López-Cortés et al., 2014). As a result, this limits the objective ability to distinguish a colonisation case from a true infection case, especially in mortality analysis.

Differences between infected and colonised patients have been previously evaluated, but cohort heterogeneity, variability in the parameters studied and/or the limited number of patients have influenced the conclusions.

A. baumannii infection or colonisation is associated with increased mortality, morbidity and longer hospital stays, also leading to higher financial costs (Young et al., 2007; Lautenbach et al., 2009). Infection control measures should be the primary measures to reduce contamination of medical equipment and devices, the incidence of patient colonisation and airborne contamination. It is necessary to follow the various guidelines on the care in intensive care, such as the use of artificial lung ventilation assist devices/equipment kits and central venous catheter care kits, especially for patients colonised with resistant microflora. It is important to evacuate invasive devices and equipment, such as an endotracheal tube or central line, as soon as possible to prevent multidrug-resistant *Acinetobacter* bacteraemia in patients colonised with this microorganism (Falagas et al., 2006; Erbay et al., 2009; Metan et al., 2009).

The study has several limitations. These could be errors in the interpretation of *A. baumannii* colonisation or infection. Most of the infections were pneumonias with relatively well-defined criteria for defining infection, whereas a large proportion of the colonisation samples were from wounds or screening material without a clearly defined clinical picture. The number of patients in the study was 90, which is relatively higher than some studies (Playford et al., 2007) but lower than other studies (Corbella et al., 2000; Jang et al., 2009), so it is likely that the deviations will be difficult to interpret.

Conclusions

1 Resistant *A. baumannii* was re-identified 12 months after the primary infection, but *A. baumannii* was no longer identified 18 months after the primary infection.

2 Risk factors for carriage of resistant *A. baumannii* after hospital discharge include infection with *A. baumannii* during the primary hospitalisation and hospital manipulations and factors.

3 Resistant *A. baumannii* most commonly causes pneumonia, bloodstream infection and surgical wound infection.

4 Risk factors for infection with resistant *A. baumannii* include hospital manipulation and factors (central line, urinary catheter, nasogastric probe, VAC system, artificial lung ventilation, haemodialysis, surgery during hospitalisation, bronchoscopy and presence of other invasive devices) and antimicrobial treatment prior to *A. baumannii* infection.

5 *A. baumannii* identified in the clinical material caused clinical manifestations of infection in 33 % of cases.

6 *A. baumannii* was most frequently identified as a colonising microorganism from bronchial lavages and wounds of different localisation.

7 Whole genome sequencing of *A. baumannii* demonstrated that *A. baumannii* identified at the time of primary infection was identical to *A. baumannii* identified during dynamic surveillance in the same patient.

Proposals

1 To add to the hospital's infection control package a recommendation to perform *A. baumannii* screening by the sponge method in patients with the following risk factors:

1.1 infection with *A. baumannii* within the last 12 months;

1.2 the patient has had the following risk factors in the last 12 months:

- central venous catheter;
- urinary catheter;
- nasogastric probe;
- VAC system;
- artificial lung ventilation;
- haemodialysis;
- surgery;
- bronchoscopy;
- presence of other invasive devices.

2 The hospital's antimicrobial guidelines be updated to include the use of antimicrobials for the treatment of infections commonly caused by *A. baumannii* (pneumonia, bloodstream infection, surgical wound infection).

3 To develop (potentially with AI assistance/support) a predictive model of the clinical presentation of *A. baumannii* infection based on the date of *A. baumannii* identification, antimicrobial therapy prior to *A. baumannii* identification and patient gender.

List of publications on the topic of the Thesis

Publications:

1 Liepiņš, M., Sīmanis, R., Lejnieks, A. 2016. Decreasing prevalence of multidrug-resistant *Acinetobacter baumannii* in Riga East university hospital. *Proceedings of the Latvian Academy of Sciences*. Section B, Vol. 70 (2016), No. 4 (703), 20–30.

2 Liepiņš, M., Krūmiņa, A. Meistere, I., Kosjkina, D., Ķibilds, J., Valciņa, O., Lejnieks, A. 2021. Retrospective study of genetic diversity of *Acinetobacter baumannii* -resistant strains isolated from patients in Riga East University Hospital in Latvia. *Proceedings of the Latvian Academy of Sciences*. Section B. Natural, Exact, and Applied Sciences. Vol. 75, no. 2, 142–148 . https://doi.org/10.2478/prolas-2021-0022 ISSN: 2255-890X

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Annexes

Annex 1

Patient questionnaire

Duration of carriage of multidrug-resistant *Acinetobacter baumannii* and its impact on infection control measures and antimicrobial use

Patient questionnaire

Background

Gender:

Female	
Male	

Age (years):

Date of first hospitalisation:

Place of hospitalisation:

	Yes	No
Intensive care		

Initial diagnosis/underlying condition:

	Yes	No
Sepsis/severe bacterial infection		
Polytrauma/trauma		
Stroke/cerebral haemorrhage		
Other		

Comorbidities:

	Yes	No
Chronic heart failure		
Chronic renal failure		
Diabetes mellitus		
Oncological disease		

Chronic wound:

Yes	No

History of risk factors:

	Yes	No
Previous hospitalisation (within the last year)		
Outpatient visit (in the last year)		
Both hospitalisation and outpatient visit		
Clients of a social care institution		

Hospital risk factors:

	Yes	No
Central line catheter		
Urinary catheter		
Nasogastric probe		
VAC system		
Artificial lung ventilation		
Haemodialysis		
Another invasive device (tracheostomy, nephrostomy, ventriculostomy, PEG, etc.)		
Surgery during hospitalisation		
Bronchoscopy		

Fatal outcome:

Yes	No

***Acinetobacter baumannii* data**

Date of first identification:

Antibacterial resistance:

	Sensitive	Resistant	Sensitive	Resistant
Amikacin				
Colistin				

Site of first release (localisation):

	Yes	No
Blood		
Urine		
Bronchial lavages		
Wound		
Liquor		
Other material (from bone, screening, etc.)		

Re-distribution time:

	After discharge	1 month	3 month	6 month	12 month	18 month
Yes						
No						

***Acinetobacter baumannii* infection/colonisation during initial hospitalisation**

	Yes	No
Colonisation		
Bone-joint infection		
Bloodstream infection		
Central nervous system infection		
Respiratory tract infection		
Surgical wound infection		
Urinary tract infection		

Antibacterials

Use of antibacterial agents before detection of *A. baumannii*:

	Yes	No
Do not use		
1 medicine		
2 medicines		
3 medicines		
Medicines not known		

Classes of antibacterial agents prior to detection of *A. baumannii*:

	Yes	No
3rd generation cephalosporins		
Antipseudomonal fluoroquinolones		
Beta-lactamase inhibitor antipseudomonal penicillins		
Carbapenems		
Polymyxins		
Other		