SCUOLA DI DOTTORATO
UNIVERSITÀ DEGLI STUDI DI MILANO-BICOCCA

Department of Medicine and Surgery

PhD program in Public Health **Cycle XXXVIII°**

Curriculum Health Technology Assessment

A network analysis of the impact of the SARS-CoV-2 pandemic on hospital robustness to antibiotic-resistant bacteria

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ACADEMIC YEAR 2024/2025

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Abbreviations

ACTs: Artemisinin-Based Combination Therapies

AIFA: Agenzia Italiana del Farmaco

AMR: Antimicrobial Resistance

ARB: Antibiotic-Resistant Bacteria

ARDS: Acute Respiratory Distress Syndrome

ART: Antiretroviral Therapy

ASST: Azienda Socio Sanitaria Territoriale

CAUTI: Catheter-Associated Urinary Tract Infections

CDC: Centers for Disease Control and Prevention

CLABSI: Central Line-Associated Bloodstream Infection

COVID-19: Coronavirus Disease 2019

DALYs: Disability Adjusted Life Years

DDD: Defined Daily Doses

EARS-Net: European Antimicrobial Resistance Surveillance Network

ECDC: European Centre for Disease Prevention and Control

EMA: European Medicines Agency

ESAC-Net: European Surveillance of Antimicrobial Consumption Network

EU/EEA: European Union/European Economic Area

FAO: Food and Agriculture Organization of the United Nations

GDP: Gross Domestic Product

GLASS: Global Antimicrobial Resistance and Use Surveillance System

GOMN: Grande Ospedale Metropolitano Niguarda of Milan

HCAIs: Healthcare-associated infections

HICC: Hospital Infection Control Committee

HIV: Human Immunodefiency Virus

HIVDR: HIV drug resistance

IPC: Infection Prevention and Control

MDR-TB: Multidrug-resistant Tuberculosis

MRSA: Methicillin-Resistant Staphylococcus Aureus

NTDs: Neglected Tropical Diseases

OECD: Organization for Economic Cooperation and Development

PPE: Personal Protective Equipment

PPS: Point Prevalence Survey

ROI: Return-on-investment

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2

SSI: Surgical Site Infections

TB: Tuberculosis

UHZ: Universitäts-Herzzentrum Freiburg – Bad Krozingen

UKF: Universitätsklinikum Freiburg

UN: United Nations

UNEP: United Nations Environment Programme

USD PPP: United States Dollar at Purchasing Power Parity

WAAW: World AMR Awareness Week

WHO: World Health Organization

WOAH: World Organisation for Animal Health

XDR-TB: Extensively drug-resistant Tuberculosis

List of tables and figures

Abstract – English

Background

Patient transfers between hospital departments and wards frequently occur and bring with them the risk of inter-department transmission of antibiotic-resistant bacteria (ARB). These bacteria form a risk to the patients already susceptible to colonisation and infection.

Aim

Goal of this study is to assess the impact of the SARS-CoV-2 pandemic on the intra-hospital network of a German and an Italian hospital.

Methods

Using data collected from the hospital between 2019 and 2023 we developed a model to represent an intra-hospital transfer network with all patient movements among all the wards, by creating a time-sliced temporal network for each month. We described the network and assessed its robustness against ARB spread by simulating outbreaks among wards.

Findings

Over the years studied, in the German hospital we found that in April 2020, when many elective surgeries were cancelled due to the SARS-CoV-2 pandemic, the robustness of the network strongly increased in comparison to all other months. Despite the network being relatively stable over the study period, it was affected by an internal change of hospital structure due to a hospital merging event. In the Italian hospital the robustness in April 2020 was stable but was lower in October 2020. This network analysis shows that network robustness tends to increase with higher levels of modularity, while it decreases as the number of transfers and links grows.

Conclusion

The intra-hospital transfer network in the German Hospital was affected by external influences due to the pandemic, slowing down the potential spread of the nosocomial pathogens; the network was generally stable and quickly recovered, although an internal force affected the structure of the network. The simulation conducted among the Italian network helped underline that network's structure influences robustness independently from number of transfers. This study advances our understanding of how antimicrobial resistance can spread through hospital networks, highlighting the importance of both structural and operational variables. A better understanding of the influence of patient transfers will help to design intervention strategies against the spread of antimicrobial resistance within hospitals.

Keywords

Antibiotic resistance, hospital networks, SARS-CoV-2, patient transfers

Abstract – Italiano

Introduzione

I trasferimenti di pazienti tra reparti e unità ospedaliere sono eventi frequenti, ma comportano un rischio significativo di trasmissione inter-reparto di batteri resistenti agli antibiotici (ARB). Tali batteri rappresentano una minaccia per i pazienti già suscettibili alla colonizzazione e all'infezione.

Obiettivi

Lo scopo del presente studio è valutare l'impatto della pandemia da SARS-CoV-2 sulla rete intraospedaliera di un grande ospedale universitario tedesco e di un ospedale italiano.

Materiali e metodi

Utilizzando i dati raccolti tra il 2019 e il 2023, è stato sviluppato un modello per rappresentare la rete di trasferimenti intraospedalieri, includendo tutti gli spostamenti dei pazienti tra le unità operative. È stata costruita una rete temporale suddivisa per mese e analizzata in termini di struttura; si è poi analizzata la sua robustezza rispetto alla diffusione di ARB, simulando focolai tra i reparti.

Risultati

Nel corso del periodo analizzato, nell'ospedale tedesco si è osservato che nel mese di aprile 2020, quando molti interventi chirurgici elettivi furono cancellati a causa della pandemia, la robustezza della rete aumentò significativamente rispetto a tutti gli altri mesi. Sebbene la rete si sia mantenuta relativamente stabile nel tempo, essa ha subito un'alterazione strutturale dovuta a un processo di fusione ospedaliera. Nell'ospedale italiano, la robustezza della rete ad aprile 2020 si è mantenuta stabile, mentre è risultata inferiore nel mese di ottobre 2020. Questa analisi della rete mostra che la robustezza tende ad aumentare al crescere della

modularità della rete e a diminuire con l'aumento del numero di trasferimenti e di collegamenti.

Conclusioni

La rete intraospedaliera dell'ospedale tedesco è stata influenzata da fattori esterni legati alla pandemia, che hanno temporaneamente rallentato la potenziale diffusione di patogeni nosocomiali; la rete ha comunque mostrato un'elevata stabilità e un rapido ritorno alla configurazione originaria, nonostante un cambiamento interno ne abbia modificato la struttura. La simulazione effettuata sulla rete dell'ospedale italiano ha evidenziato che la struttura della rete influenza la robustezza in modo indipendente rispetto al solo numero di trasferimenti. Il presente studio contribuisce a migliorare la comprensione delle dinamiche di diffusione della resistenza antimicrobica all'interno delle reti ospedaliere, mettendo in luce l'importanza delle variabili sia strutturali sia operative. Una comprensione più approfondita dell'impatto dei trasferimenti di pazienti potrà supportare la progettazione di strategie di intervento più efficaci contro la diffusione della resistenza antimicrobica in ambito ospedaliero.

Parole chiave

Resistenza agli antibiotici, reti ospedaliere, SARS-CoV-2, trasferimenti di pazienti

1. Introduction

1.1 Healthcare-associated infections

1.1.1 Definition

Healthcare-associated infections (HCAIs) are infections that are not present or incubating at the time of admission that patients acquire in various settings while or soon after obtaining health care, meaning not only in acute-care hospital but also in long-term care, family medicine clinics, and ambulatory care [1], [2]. Originally, infections associated with hospital stays were referred to as 'nosocomial infections,' but starting in the 1990s, with the expansion of extra-hospital care settings, it became necessary to broaden the concept to include healthcare and social care–associated infections [1]. Infections are considered HCAIs if they first appear 48 hours or more after hospital admission or healthcare treatment or within 30 days after having received healthcare [1].

HCAIs can be caused by different germs, such as Methicillin-Resistant Staphylococcus Aureus (MRSA), and the most frequently reported ones can include respiratory tract infections, Surgical Site Infections (SSI), Catheter-Associated Urinary Tract Infections (CAUTI), Central Line-Associated Bloodstream Infection (CLABSI) and gastro-intestinal infections [3], [4].

HCAIs may represent a serious threat to healthcare safety: even though some of these infections can be treated easily, others may more seriously affect a patient's health [4]. In recent years, significant attention has been devoted to the prevention and control of these infections due to a steadily increasing epidemiological trend, which has serious implications for patient health, as well as psychological and financial consequences [2]. These include prolonged hospital stays and hospital costs, long-term disability, increased mortality, and the spread of antibiotic resistance, among others [2]. The rise in HCAIs might have been influenced

by multiple factors, such as the spread of antibiotic-resistant microorganisms and the progressive introduction of new medical technologies.

1.1.2 Epidemiology

According to the Istituto Superiore di Sanitá, in a prevalence study conducted in 56 acute care hospitals (which includes all healthcare facilities providing short-term care) in Italy in 2016 1,186 out of a total of 14,773 patients (8,03%) presented at least one HCAI, with a total number of HCAIs of 1,296; among these, the most frequently reported infections were respiratory tract infections (22.8%), bloodstream infections (18.3%), urinary tract infections (18%), and surgical site infections (14.4%) [2]. Regarding the microorganisms involved, 67 different pathogen types were identified: of these, Escherichia coli (13%), Klebsiella pneumoniae (10.4%), Pseudomonas aeruginosa (8.1%), Staphylococcus aureus (8.9%), and Staphylococcus epidermidis (6.3%) accounted for over 45% of all isolates, and were often found to be multidrug-resistant [2].

More than 4.2 million cases of HCAIs are estimated to occur in hospitals in the European Union and European Economic Area (EU/EEA) each year [5] as shown in Figure 1, considering that HCAIs constitute 71% of cases of infections with antibiotic-resistant bacteria, including bacteria resistant to last-resort antibiotics, such as carbapenem-resistant Enterobacterales [6]. Furthermore, 7.1% of patients in hospitals have at least one HCAI (Figure 2) [5]. According to the World Health Organization (WHO) report in 2022 8.9 million HCAIs occur every year in acute and long-term care facilities in EU/EEA [7].

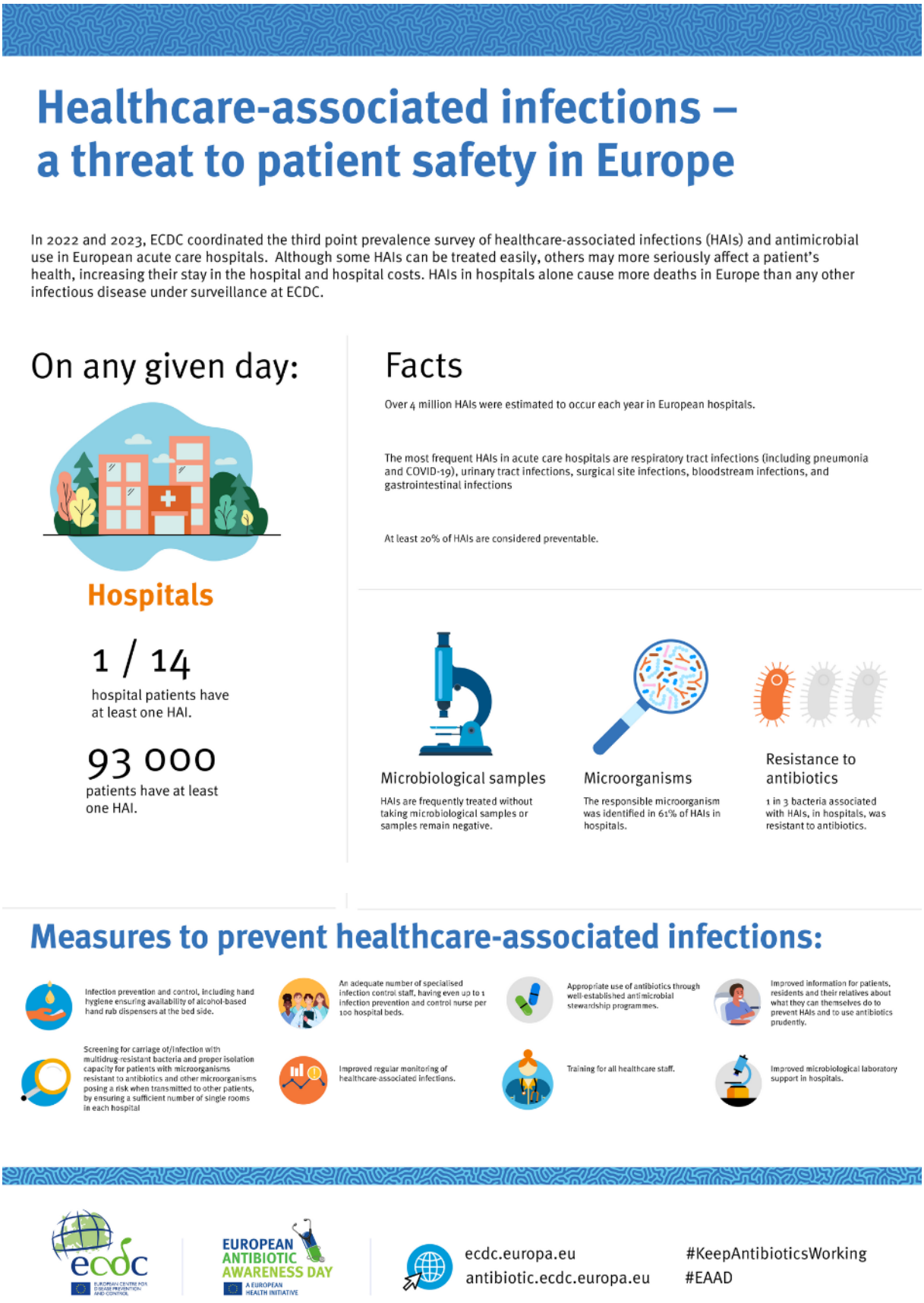

***Figure 1**. Healthcare-associated infecitons in Europe and measures to prevent them. Source available: https://www.ecdc.europa.eu/en/publications-data/healthcare-associated-infections-threat-patient-safety-europe*

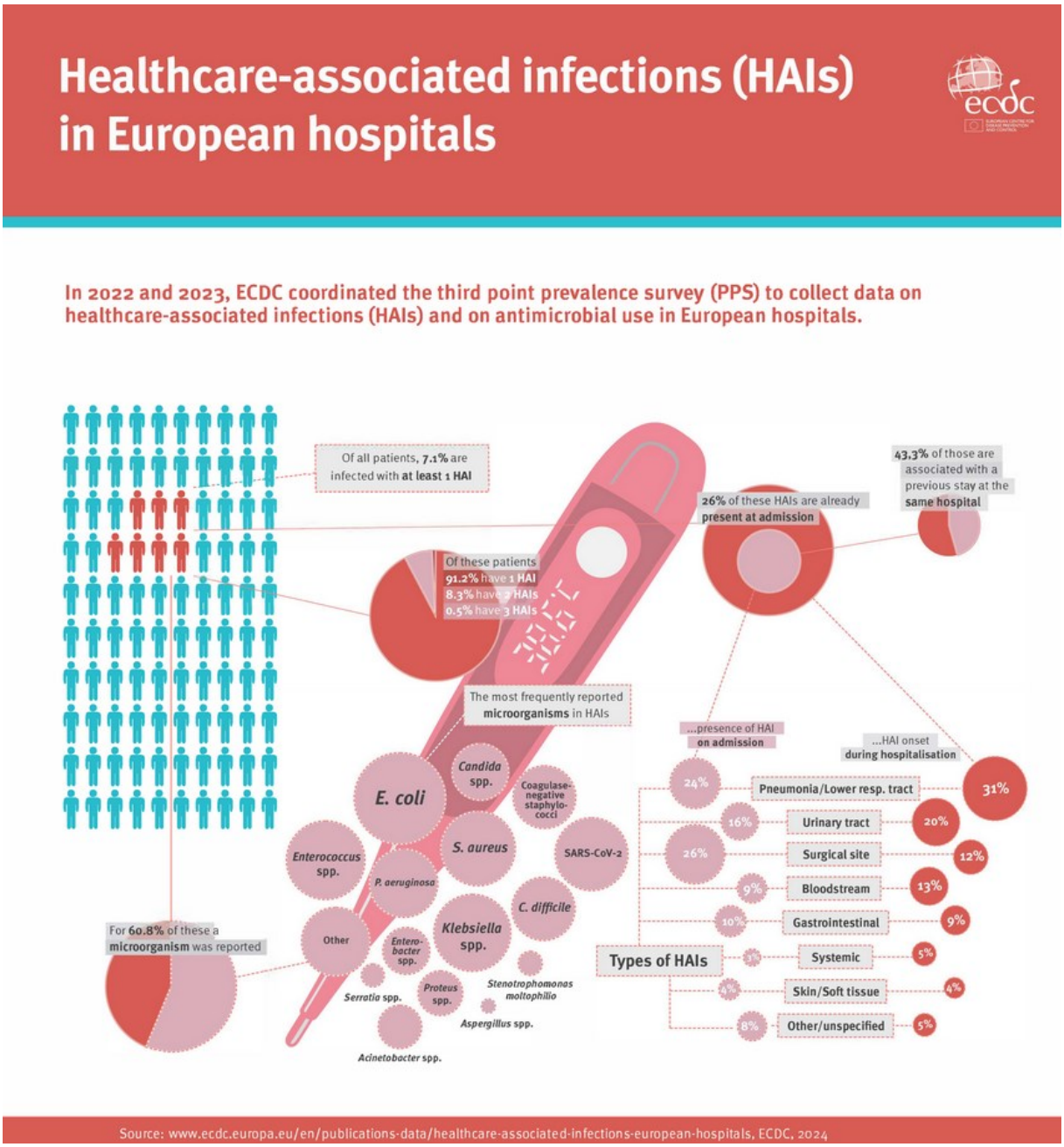

***Figure 2**. Healthcare-associated infecitons in European hospitals. Source available: https://www.ecdc.europa.eu/en/publications-data/healthcare-associated-infections-european-hospitals-pps-survey-2022-2023*

According to the Centers for Disease Control and Prevention (CDC) in 2015 in U.S. acute care hospitals there were an estimated 687,000 HCAIs [8]. On average, around 1 in 10 patients is affected by HCAIs [9]; the frequency is estimated to be higher in low-/middle-income countries and in high-risk patients such as those in intensive care unit [9]. According to research published by Balasubramanian et al., an estimated 136 million cases of health care-associated antibiotic resistant infections occur worldwide every year [9].

1.1.3 Transmission modalities

The transmission of infection in healthcare settings requires three essential elements: an infectious microorganism, a susceptible host, and a way of transmission from the microorganism to the host [1], [2]. Transmission of HCAIs, as other infections, depends on the specific microorganism involved and may occur through various mechanisms [2]:

- Direct contact between an infected individual and a healthy person, particularly via the hands of healthcare workers
- Droplet transmission, through respiratory droplets expelled by an infected person during coughing or sneezing
- Airborne transmission, involving small microorganisms that remain suspended in the air for extended periods
- Indirect contact via contaminated vehicles, such as endoscopes or surgical instruments

Multiple factors contribute to HCAIs including [10]:

- healthcare associated factors, such as the use of invasive devices, surgical procedures, and selection pressure from excessive antibiotic use
- environmental factors, such as contaminated air-conditioning systems and the physical layout of the facility (e.g., open units with beds close together)
- patient-related factors, such as severity of underlying illness, use of immunosuppressive agents, and prolonged hospital stays.

These factors interact and multiple factors may play a role including staffing (e.g., nurse-to-patient ratio) and the lack of effective intervention programs designed to reduce HCAIs [10].

Individuals at risk of HCAIs are primarily patients, although healthcare personnel may also be affected, albeit less frequently [2]. The factors that predispose individuals to HCAIs can be classified as extrinsic, intrinsic, or related to predisposing care practices [2].

Extrinsic risk factors include [2]:

- Length of hospital stay (prolonged hospital stays are associated with a higher probability of contracting an infection; it is important to consider that the true incidence of HCAIs may be underestimated, as the length of stay can be shorter than the incubation period of the infecting microorganism, and symptoms may appear days after discharge)
- Use of invasive devices (e.g., peripheral or central venous catheters, urinary catheters, intubation)
- Admission to intensive care units
- Surgical procedures

Intrinsic risk factors include [2]:

- Age (particularly neonates and the elderly)
- Gender (higher risk observed in males)
- Presence of other infections or severe comorbid conditions (e.g., cancer, immunodeficiency, diabetes, disability, obesity, respiratory or gastrointestinal disorders, body temperature >38°C at admission)
- Trauma or burns
- Altered level of consciousness

Risk factors related to care practices, settings, or specific microorganisms include catheter-associated urinary tract infections, infections linked to endoscopic procedures, infections linked to central vascular catheters and others [2].

1.1.4 Antimicrobial resistance

Antimicrobials, which include antibiotics, antivirals, antifungals, and antiparasitics, are essential medications used to prevent or treat infectious diseases in humans, animals, and plants. However, the effectiveness of these drugs is increasingly threatened by antimicrobial resistance (AMR), a phenomenon in which bacteria, viruses, fungi, and parasites evolve to resist the effects of antimicrobial agents [11].

As resistance develops, treatments become less effective or even obsolete, making infections more difficult to manage. This leads to increased transmission of disease, more severe health outcomes, prolonged illness, higher rates of disability, and elevated mortality [11].

Although AMR arises naturally over time through genetic mutations in microorganisms, its development and global spread have been significantly accelerated by human practices. Chief among these are the misuse and overuse of antimicrobials in the treatment, prevention, and control of infections across human, veterinary, and agricultural sectors [11].

AMR is a problem for all countries at all income levels. Contributing factors include lack of access to clean water, sanitation and hygiene for both humans and animals; poor infection and disease prevention and control in homes, healthcare facilities and farms; poor access to quality and affordable vaccines, diagnostics and medicines; lack of awareness and knowledge; and lack of enforcement of relevant legislation [11]. People living in low-resource settings and vulnerable populations are especially impacted by both the drivers and consequences of AMR.

Antibiotic-Resistant Bacteria

The increasing prevalence of antibiotic-resistant bacteria represents a major global health threat, as the effectiveness of standard treatments against common infections continues to decline. In Figure 3, the European Centre for Disease Prevention and Control (ECDC) reported data on HCAIs and on antimicrobial use in European hospitals, showing the percentage of specific bacteria resistant to different antibiotics.

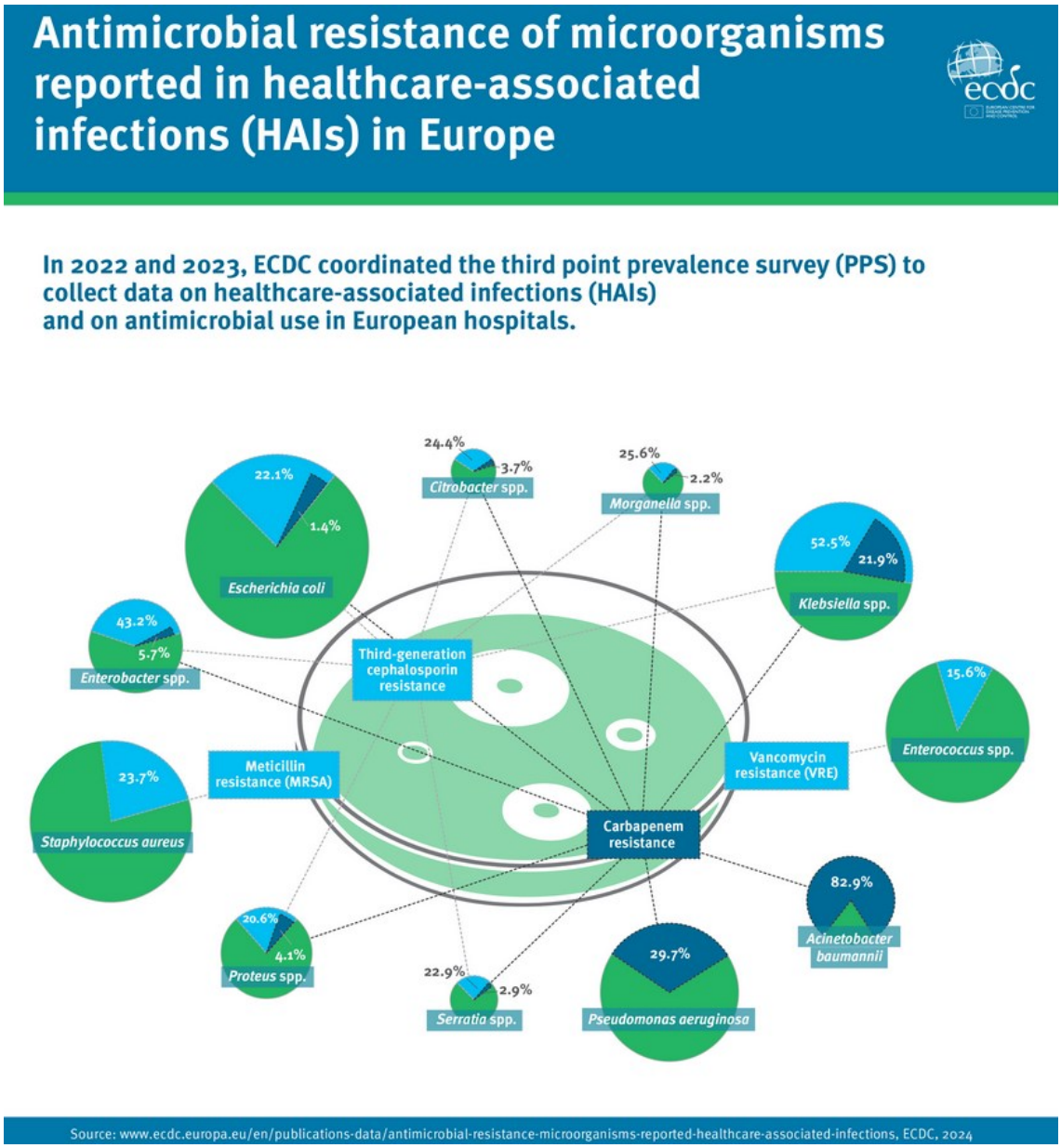

***Figure 3**. Antimicrobial resistance of microorganisms reported in healthcare-associated infections in Europe. Source available: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-resistance-microorganisms-reported-healthcare-associated-infections*

According to the 2022 Global Antimicrobial Resistance and Use Surveillance System (GLASS) report [12], alarmingly high resistance rates have been documented in numerous countries. Data from 76 nations indicate that resistance to third-generation cephalosporins in *Escherichia coli* has reached a median of 42%, while Methicillin-Resistant *Staphylococcus aureus* (MRSA) accounts for 35% of cases. Infections such as urinary tract infections caused by *E. coli* are increasingly unresponsive to first-line treatments including ampicillin, co-trimoxazole, and fluoroquinolones, complicating clinical management [12].

Similarly, *Klebsiella pneumoniae*, a common gut bacterium, is displaying heightened resistance to crucial antibiotics, prompting increased reliance on carbapenems—often considered the treatment of last resort. However, resistance to these drugs is also rising in various regions. The Organization for Economic Cooperation and Development (OECD) [13] predicts that resistance to such last-line therapies may double by 2035 compared to 2005 levels (Figure 4), emphasizing the urgency of scaling up antimicrobial stewardship and global surveillance systems.

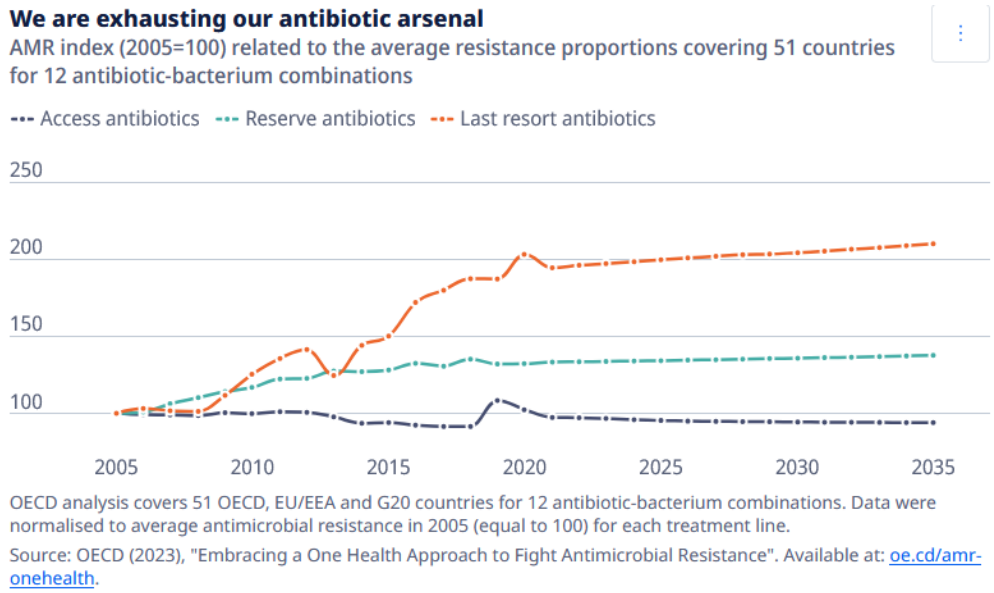

***Figure 4**. AMR predictions until 2035 and access antibiotics, reserve antibiotics and last resort antibiotics. Source available: https://www.oecd.org/en/topics/antimicrobial-resistance.html*

Fungal Resistance

The escalation of antifungal resistance is an emerging challenge being closely monitored by both the WHO and the ECDC. Treating fungal infections can be particularly difficult due to drug interactions, especially in immunocompromised patients such as those living with Human Immunodeficiency Virus (HIV). WHO's creation of the Fungal Priority Pathogens List [14] reflects a systematic evaluation of the global burden and resistance patterns of fungal infections.

One major concern is the global spread of the multidrug-resistant pathogen *Candidozyma auris* (formerly *Candida auris*), a serious cause of invasive fungal disease. Recent surveillance updates from the European Centre for Disease Prevention and Control [15] further highlight the growing public health relevance of *C. auris* in Europe. The organism continues to spread rapidly, with Germany and Italy among the countries reporting notable increases in the number of infections. According to the most recent ECDC survey, distinct *C. auris* outbreaks were documented in Cyprus, France and Germany, whereas four countries (Greece, Italy, Romania and Spain) reported that specific outbreaks could no longer be distinguished due to the establishment of regional endemicity. Despite the observed increase, the recorded case numbers are likely to represent only the tip of the iceberg, as systematic surveillance is not in place in many European countries. These findings underscore the urgent need for strengthened infection-prevention measures, enhanced laboratory capacity for rapid identification, and coordinated regional surveillance systems to curb the further spread of this pathogen in hospital settings.

Resistance in HIV, Tuberculosis, and Malaria

Drug resistance is also a growing problem in the management of HIV, tuberculosis (TB), and malaria. In the case of HIV, resistance develops either through direct transmission of resistant strains or as a result of poor adherence to antiretroviral therapy (ART), including issues arising from drug interactions. HIV drug resistance (HIVDR) compromises treatment outcomes and contributes to increased morbidity and mortality. WHO advises regular HIVDR monitoring to guide optimal treatment choices [16].

Tuberculosis remains one of the leading contributors to antimicrobial resistance [11]. Multidrug-resistant TB (MDR-TB), characterized by resistance to isoniazid and rifampicin, is treatable but requires second-line medications that are more toxic, expensive, and less effective. Extensively drug-resistant TB (XDR-TB), involving resistance to key second-line agents, presents even fewer treatment options. Alarmingly, only about 40% of patients diagnosed with drug-resistant TB received appropriate therapy in 2022, posing a serious threat to public health and disease control efforts [11].

Malaria control efforts are similarly at risk due to emerging resistance in *Plasmodium falciparum* to artemisinin-based combination therapies (ACTs), the most widely used treatment [4], [11]. Partial resistance to artemisinin or its partner drugs has been detected in regions such as the Greater Mekong Subregion and parts of the Eastern Mediterranean and Africa. While current ACTs remain effective in most cases, ongoing mutations and resistance spread could jeopardize malaria treatment strategies, highlighting the need for continuous monitoring and updated therapeutic guidelines [11].

Drug Resistance in Neglected Tropical Diseases (NTDs)

Antimicrobial resistance is also affecting the management of neglected tropical diseases (NTDs), which predominantly impact marginalized and underserved populations [11]. Resistance has been reported against key drugs used to treat diseases like leprosy (e.g., rifampicin, dapsone), human African trypanosomiasis (e.g., melarsoprol), and leishmaniasis (e.g., miltefosine, pentavalent antimonials) [11]. Effective surveillance, prudent drug use, and the development of alternative treatments are essential to preserving treatment efficacy. WHO continues to support global and national initiatives aimed at tracking resistance and guiding the safe, standardized administration of medicines, including those donated for NTD programs [11].

1.1.5 Antimicrobial use

Antimicrobial consumption across Europe and all over the world remains a significant public health concern, closely monitored by the European Centre for Disease Prevention and Control and WHO. Based on data from the third point prevalence survey conducted by the European Centre for Disease Prevention and Control in European acute care hospitals in 2023–2024 [17], it appears that antibiotics, which are frequently used in hospital settings, may at times be administered unnecessarily (Figure 5). Specifically, one in three patients received at least one antimicrobial on any given day, one in ten antimicrobial prescriptions were for medical prophylaxis — for which only a limited number of indications are recommended — and half of the surgical prophylaxis prescriptions were administered for more than a single dose, which is usually sufficient. These practices further contribute to the spread of antimicrobial resistance.

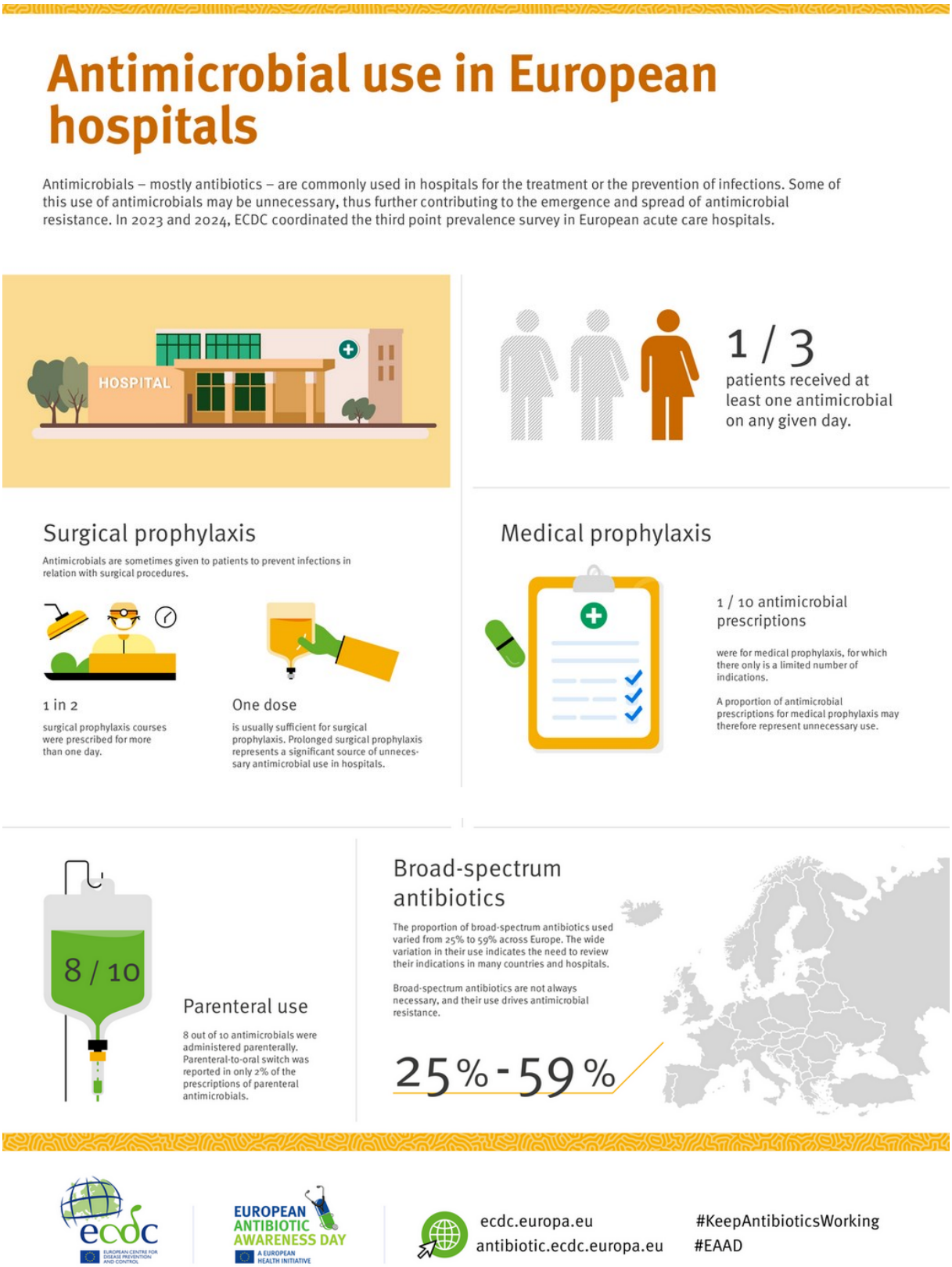

Figure 5. *Antimicrobial use in European hospitals. Source available:* https://www.ecdc.europa.eu/en/publications-data/antimicrobial-use-european-hospitals-2022-2023

To try to offer a guide in antibiotics prescriptions, the WHO AWaRe (Access, Watch, Reserve) antibiotic book [18] provides concise, evidence-based guidance on the choice of antibiotic, dose, route of administration, and duration of treatment for more than 30 of the most common clinical infections in children and adults in both primary health care and hospital settings.

Antibiotics are divided in three cathegories, “Access”, “Watch” and “Reserve” antibiotics [19]. Their definitions are as follows [19]:

- Access: antibiotics with a narrow spectrum of activity, generally with less side-effects, a lower potential for the selection of antimicrobial resistance and of lower cost. They are recommended for the empiric treatment of most common infections and should be widely available.
- Watch: generally, have a higher potential for the selection of antimicrobial resistance and are more commonly used in sicker patients in the hospital facility setting. Their use should be carefully monitored to avoid overuse.
- Reserve: last-resort antibiotics that should only be used to treat severe infections caused by multidrug-resistant pathogens.

WHO and others are increasingly employing the AWaRe classification to monitor antibiotic use and support antimicrobial stewardship activities [19].

According to the 2023 Annual Epidemiological Report, the combined community and hospital sector consumption of antibacterials for systemic use (ATC group J01) in the EU/EEA was 20.0 defined daily doses (DDD) per 1,000 inhabitants per day (Figure 6) [20]. This figure exceeds

the EU's 2030 target, as shown in Figure 6, which is 15.9 DDD per 1,000 inhabitants per day, indicating a need for intensified efforts to reduce unnecessary antibiotic use [20].

Define Daily Dose (DDD)

The apparently simplest way to measure the volume of drug prescriptions is to count the number of packages prescribed and, possibly, group them by active ingredient or therapeutic group. However, this method has significant limitations that discourage its use. For the same drug, the various formulations on the market may differ in the number of dosage units contained: packages of the same drug with a different number of tablets will always be counted as one unit, even though the number of individual doses provided to the patient is different. Even when comparing different molecules within a therapeutic group, counting the number of packages can provide a distorted measure of drug exposure. A typical example is the comparison between an oral antibiotic such as amoxicillin and an injectable one such as piperacillin. In the first case, one package provides several days of therapy; in the second case, multiple packages (usually containing only one vial each) may be required for just one day of therapy.

To overcome these issues, drug consumption is measured using the DDD, which has become the international standard unit for pharmaceutical prescription. Through the DDD, data are expressed as the number of “conventional” days of prescribed therapy and thus allow for direct comparison between drugs used at different doses (due to differing pharmacological potency) or with different indications. The DDD is defined as the average dose of a drug taken daily by an adult patient, with reference to the drug’s main therapeutic indication [21]. Therefore, the DDD represents the maintenance dose of the therapy and not the initial dose. It is important not to assign an improper meaning to the DDD, neither as a recommended nor

as a prescribed dose: it should be regarded solely as a technical tool for measuring drug prescriptions. It should be emphasized that the actual daily dose used in the treatment of patients, whether in hospital or in outpatient settings, may differ from the DDD. For example, the DDD assigned to the antibiotic amoxicillin is 1 gram, whereas the actual daily dose used can vary from 1 to 3 grams or more, depending on the type and severity of the infection being treated. DDDs provide a fixed unit of measurement independent of price, currencies, package size and strength, enabling the researcher to assess trends in drug utilization and to perform comparisons between population groups.

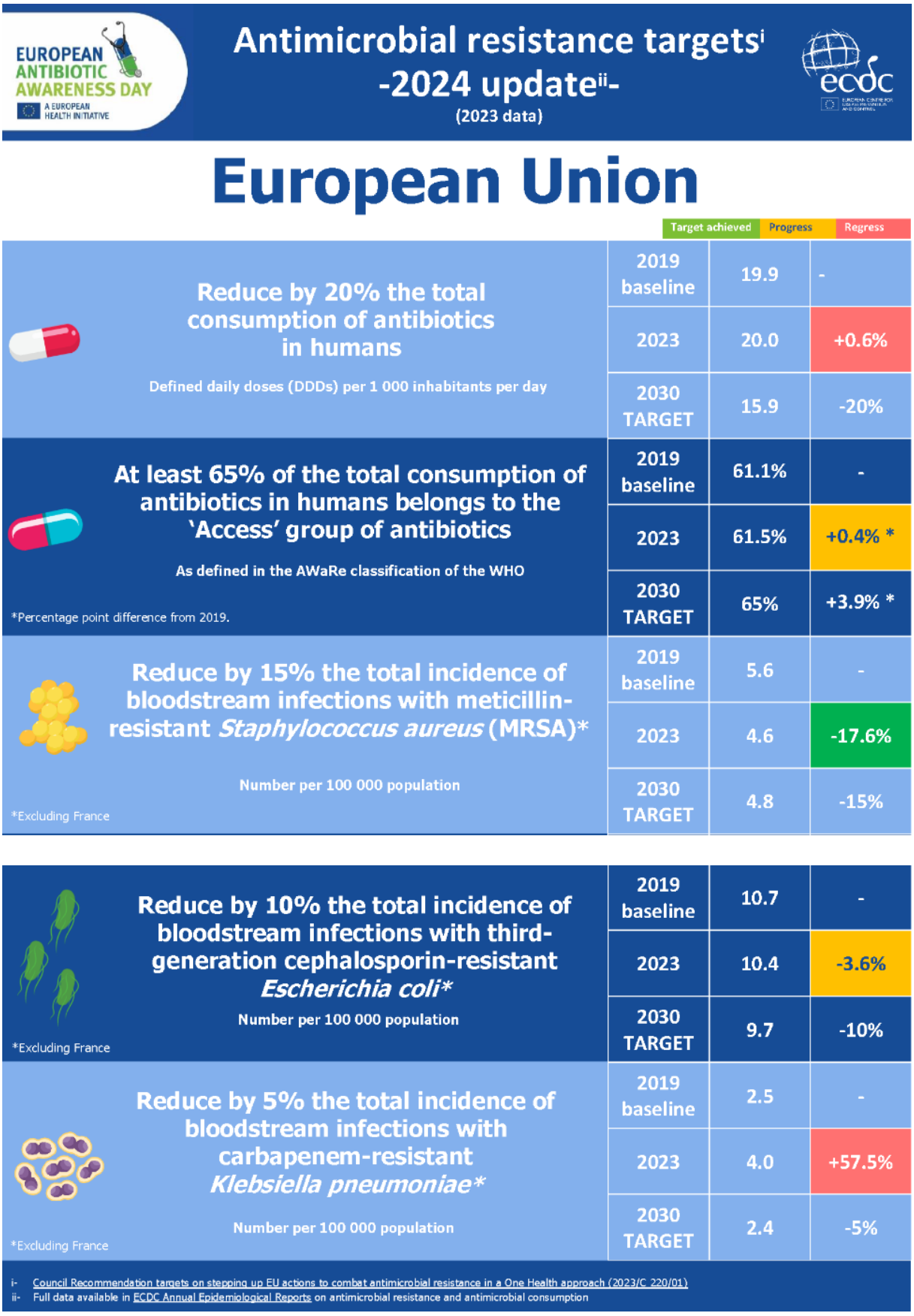

Figure 6. *European antimicrobial resistance targets. Source available: https://antibiotic.ecdc.europa.eu/en/publications-data/infographic-antimicrobial-resistance-targets-how-eu-doing-2024-update*

In the primary care sector, the EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) was 18.3 DDD per 1 000 inhabitants per day (country range: 8.8–26.7) in 2023, with no statistically significant trend between 2019 and 2023 for the EU/EEA overall [20]. At EU/EEA level, the most consumed subgroup of antibiotics was penicillins (J01C) (47%), followed by macrolides, lincosamides and streptogramins (J01F) (17%), cephalosporins and other beta-lactams (J01D) (12%), tetracyclines (J01A) (9%), quinolones (J01M) (7%), other antibacterials (J01X) (5%), sulfonamides and trimethoprim (J01E) (3%), and other groups (J01B, J01G and J01R) (0.5%); a statistically significant decreasing trend was observed between 2019 and 2023 for 'Other groups (J01B, J01G, and J01R)' [20].

In the hospital sector, the EU/EEA population-weighted mean consumption of antibacterials for systemic use (ATC group J01) was 1.6 DDD per 1 000 inhabitants per day in 2023 (country range: 0.8–3.2), with no statistically significant trend detected between 2019 and 2023 for EU/EEA overall [20]. At EU/EEA level, the most commonly consumed subgroup of antibiotics was penicillins (J01C) (34%), followed by cephalosporins and other beta-lactams (J01D) (28%), other antibacterials (J01X) (12%), quinolones (J01M) (9%), macrolides, lincosamides and streptogramins (J01F) (8%), sulfonamides and trimethoprim (J01E) (4%), other groups (J01B, J01G, and J01R) (3%) and tetracyclines (J01A) (3%) [20]. A statistically significant decreasing trend was observed at EU/EEA level between 2019 and 2023 for quinolones (J01M) and for other groups (J01B, J01G, and J01R); and a statistically increasing trend was observed for other antibacterials (J01X), which was mainly due to an increase in the consumption of polymyxins (J01XB) [20].

The poor progress towards the EU targets on antimicrobial consumption and the continued increase in the consumption of WHO 'Reserve' and 'broad-spectrum' antibiotics highlights the

need to strengthen efforts to address unnecessary and inappropriate antimicrobial use at all levels of healthcare (i.e. community, hospital and long-term care sectors) in the EU/EEA.

In the hospital setting, the ECDC's 2022–2023 Point Prevalence Survey (PPS) revealed that 35.5% of patients in European acute care hospitals were receiving at least one antimicrobial agent on the day of the survey (Figure 7) [17]. The most common indications for antimicrobial use were the treatment of community-acquired infections, healthcare-associated infections, and surgical prophylaxis [17]. Notably, over half (54.2%) of antimicrobials prescribed for surgical prophylaxis were administered for more than one day, contrary to guidelines recommending shorter durations [17].

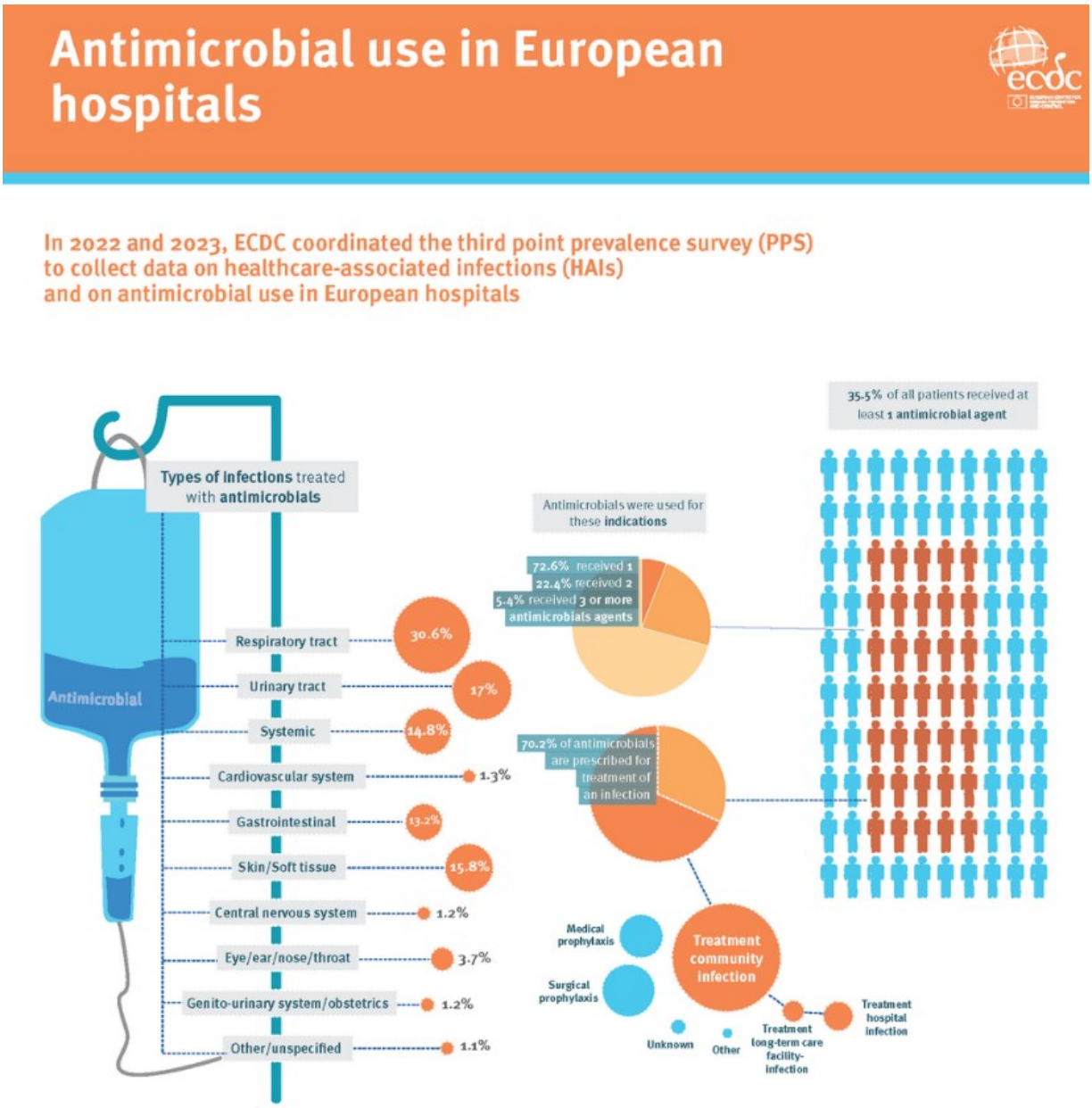

***Figure** 7. Antimicrobial use in European hospitals. Source available: https://www.ecdc.europa.eu/en/publications-data/antimicrobial-use-european-hospitals*

The ECDC also publishes detailed country-specific fact sheets that provide key indicators on antimicrobial consumption and resistance for each EU/EEA member state [5]. A comparative analysis between Germany and Italy clearly highlights significant differences, as shown respectively in Figure 8 and Figure 9: Italy shows higher levels of antibiotic consumption and lower adherence to recommended stewardship practices. These disparities underscore the urgent need for more robust interventions and policy measures in the Italian context to align with European targets and best practices in antimicrobial stewardship.

Key indicators

Point prevalence survey of healthcare-associated infections and antimicrobial use in acute care hospitals

2022-2023

GERMANY

Number of hospitals	50
Standard protocol	0
'Light' protocol	50
Number of patients	8857

	Min.	25th percentile	EU/EEA country median	75th percentile	Max.	Country
Healthcare-associated infections (HAIs) and antimicrobial resistance (AMR) indicators						
HAI prevalence* (% patients with HAI)	3.0	5.1	**6.8**	8.2	13.8	**4.2**
Composite index** of AMR (% antimicrobial-resistant isolates)	7.9	15.4	**21.8**	38.2	68.7	**17.3**
Infection prevention and control (IPC) and diagnostic stewardship indicators						
IPC nurses (full-time equivalents (FTEs) per 250 beds)	0.28	0.98	**1.25**	1.54	3.28	**1.50**
Beds with alcohol-based handrub dispenser at point of care (% beds)	18.5	43.4	**49.2**	69.7	100	**69.7**
Beds in single rooms (% beds)	3.2	7.1	**15.8**	35.2	56.5	**14.0**
Blood culture sets (number per 1000 patient-days)	12.4	28.0	**44.7**	68.9	167.1	**51.1**
Antimicrobial use (AU) and antimicrobial stewardship indicators						
AU prevalence (% patients with AU)	20.8	29.7	**36.0**	43.8	56.5	**26.2**
Duration of surgical prophylaxis >1 day (% of antimicrobials for surgical prophylaxis)	15.8	31.2	**38.1**	60.1	79.8	**28.2**
Antimicrobials reviewed and changed during treatment (%)	6.2	13.9	**19.5**	24.1	31.3	**17.5**

*HAI prevalence should be interpreted with caution, as it depends on patient mix, diagnostic capacity, sensitivity of HAI case finding and country representativeness of the sample of hospitals.

**The percentage of the sum of isolates of the following resistant microorganisms divided by the sum of the isolates for which results from antimicrobial susceptibility testing were reported: *Staphylococcus aureus* resistant to meticillin (MRSA), *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, Enterobacterales resistant to third-generation cephalosporins, and *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems.

Legend:

- Better than both EU/EEA country median and the 25th (or 75th) percentile
- Better than EU/EEA country median, but worse than the 25th (or 75th) percentile
- Worse than EU/EEA country median, but better than the 75th (or 25th) percentile
- Worse than both EU/EEA country median and the 75th (or 25th) percentile

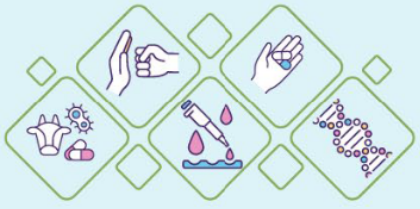

***Figure 8**. Point prevalence survey of healthcare-associated infections and antimicrobial use in acute care hospitals in 2022-2023 in Germany. Source available:https://www.ecdc.europa.eu/en/publications-data/country-factsheet-germany*

Key indicators

Point prevalence survey of healthcare-associated infections and antimicrobial use in acute care hospitals

2022-2023

ITALY

Number of hospitals	58
Standard protocol	58
'Light' protocol	0
Number of patients	19740

	Min.	25th percentile	EU/EEA country median	75th percentile	Max.	Country
Healthcare-associated infections (HAIs) and antimicrobial resistance (AMR) indicators						
HAI prevalence* (% patients with HAI)	3.0	5.1	**6.8**	8.2	13.8	**9.8**
Composite index** of AMR (% antimicrobial-resistant isolates)	7.9	15.4	**21.8**	38.2	68.7	**40.0**
Infection prevention and control (IPC) and diagnostic stewardship indicators						
IPC nurses (full-time equivalents (FTEs) per 250 beds)	0.28	0.98	**1.25**	1.54	3.28	**1.74**
Beds with alcohol-based handrub dispenser at point of care (% beds)	18.5	43.4	**49.2**	69.7	100	**54.6**
Beds in single rooms (% beds)	3.2	7.1	**15.8**	35.2	56.5	**13.5**
Blood culture sets (number per 1000 patient-days)	12.4	28.0	**44.7**	68.9	167.1	**85.3**
Antimicrobial use (AU) and antimicrobial stewardship indicators						
AU prevalence (% patients with AU)	20.8	29.7	**36.0**	43.8	56.5	**44.7**
Duration of surgical prophylaxis >1 day (% of antimicrobials for surgical prophylaxis)	15.8	31.2	**38.1**	60.1	79.8	**59.0**
Antimicrobials reviewed and changed during treatment (%)	6.2	13.9	**19.5**	24.1	31.3	**14.7**

*HAI prevalence should be interpreted with caution, as it depends on patient mix, diagnostic capacity, sensitivity of HAI case finding and country representativeness of the sample of hospitals.

**The percentage of the sum of isolates of the following resistant microorganisms divided by the sum of the isolates for which results from antimicrobial susceptibility testing were reported: *Staphylococcus aureus* resistant to meticillin (MRSA), *Enterococcus faecium* and *Enterococcus faecalis* resistant to vancomycin, Enterobacterales resistant to third-generation cephalosporins, and *Pseudomonas aeruginosa* and *Acinetobacter baumannii* resistant to carbapenems.

Legend:

- Better than both EU/EEA country median and the 25th (or 75th) percentile
- Better than EU/EEA country median, but worse than the 25th (or 75th) percentile
- Worse than EU/EEA country median, but better than the 75th (or 25th) percentile
- Worse than both EU/EEA country median and the 75th (or 25th) percentile

Figure 9. *Point prevalence survey of healthcare-associated infections and antimicrobial use in acute care hospitals in 2022-2023 in Italy. Source available: https://www.ecdc.europa.eu/en/publications-data/country-factsheet-italy*

Antimicrobial Consumption and Resistance: The Italian Context

In Europe, antibiotic consumption is monitored by the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), a network coordinated by the European Centre for Disease Prevention and Control (ECDC). Annually, ESAC-Net collects data on the consumption of systemic antimicrobials from EU and EEA countries, which are submitted to the ECDC-managed central database, EpiPulse-TESSy. These data, derived from national surveillance systems, are analyzed in terms of defined daily doses (DDD) per 1,000 inhabitants per day, utilizing Eurostat population figures for both community and hospital sectors. The data are further integrated with resistance data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) to assess correlations between antibiotic consumption and resistance rates among specific bacterial species.

According to the report released from Agenzia Italiana del Farmaco (AIFA) in 2023, Italy reported a community antibiotic consumption of 21.2 DDD per 1,000 inhabitants per day, marking a 5.7% increase compared to 2022 [22] (see Table 1). This positions Italy among the countries with the highest antibiotic usage in Europe. Notably, all therapeutic categories exhibited increased consumption relative to 2022, except for macrolides and quinolones. Italy recorded the highest increase in beta-lactam antibiotic consumption (+14.3%) in Europe, second only to Germany (+16.4%), whose absolute consumption remains less than half of Italy's [22].

Paesi UE/SEE	Totale (J01)	Δ% 23-22
Austria	9,5	7,9
Belgio	19,1	0,7
Bulgaria	24,6	1,8
Croazia	19,1	5,3
Danimarca	14,3	7,0
Estonia	11,2	3,6
Finlandia	11,1	5,7
Francia	22,3	-1,0
Germania	11,7	16,6
Grecia	26,7	-14,2
Irlanda	20,7	-3,8
Islanda	17,4	-0,6
Italia°	**21,2**	**5,7**
Lettonia	13,3	-0,6
Lituania	16,3	0,9
Lussemburgo	18,7	6,1
Malta	20,9	-3,8
Norvegia	14,2	1,5
Olanda	8,8	5,8
Polonia	21,8	-2,0
Portogallo	18,0	5,4
Rep. Ceca	15,0	7,5
Romania	25,8	-1,4
Slovacchia	19,0	-3,5
Slovenia	11,9	8,6
Spagna	22,5	3,8
Ungheria	13,1	-1,6
UE/SEE*	**18,3°°**	**2,5**

^Data generated by the European Surveillance System (ESAC-Net) and available in EpiPulse-TESSy as of 20 October 2024.
**EU/EEA: population-weighted average consumption based on all data reported for each year.
°The value does not exactly match the sum of the figures reported in Tables 2.1 (reimbursed: 15.3 DDD per 1,000 inhabitants per day) and 3.1 (private purchases: 5.3 DDD per 1,000 inhabitants per day), due to rounding approximations in the calculation.
°°Data refer to the most recent extraction as of 20 October 2024 and may therefore differ from those currently displayed on the online ESAC-Net dashboard.

***Table 1**. Territorial consumption of systemic antibiotics (DDD per 1,000 inhabitants per day) by EU/EEA country: 2022–2023 comparison^. Source available: https://www.aifa.gov.it/documents/20142/2766777/Rapporto_Antibiotici_2023.pdf*

Furthermore, Italy demonstrates excessive reliance on 'Watch' category antibiotics, which are associated with a higher potential for resistance development. Figure 10 shows that in 2023 only 52% of community antibiotic consumption in Italy pertained to 'Access' group antibiotics

[22], as per the WHO's AWaRe classification. Although this reflects an improvement from 2022, it remains significantly below the European average of 63%; only Hungary, Bulgaria, Greece, and Slovakia reported lower percentages (European Council recommended target: 65%) (Figure 10).

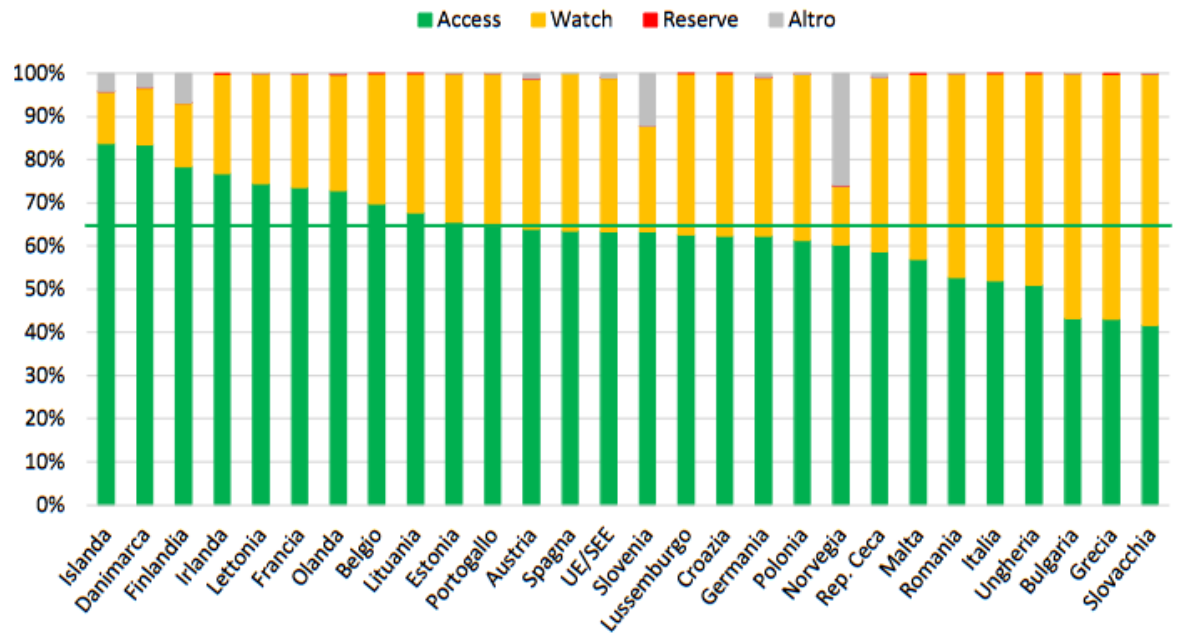

***Figure 10**. Variability by EU/EEA country in territorial consumption (DDD per 1,000 inhabitants per day) of systemic antibiotics (J01) by WHO AWaRe classification in 2023. Source available: https://www.aifa.gov.it/documents/20142/2766777/Rapporto_Antibiotici_2023.pdf*

In the hospital sector (Table 2), Italy's antibiotic consumption in 2023 was 1.9 DDD per 1,000 inhabitants per day, exceeding the European average of 1.6 DDD and representing a 5.0% increase from 2022 [22]. Only Croatia, the Czech Republic, Denmark, Lithuania and Malta reported higher hospital antibiotic consumption (Table 2). The most significant increases in Italy were observed in sulfonamides combined with trimethoprim (+11.6%) and macrolides (+6.7%); beta-lactam antibiotics, including penicillins, also showed increased usage, while quinolone consumption continued to decline (-2.7% in Italy), aligning with EMA and AIFA recommendations [22].

Paesi UE/SEE	Totale (J01)	Δ% 23-22
Austria	1,78	5,2
Belgio	1,48	0,1
Bulgaria	1,66	11,0
Croazia	2,08	4,9
Germania	1,65	0,0
Danimarca	1,91	4,6
Estonia	1,54	-4,4
Finlandia	1,84	-7,1
Francia	1,72	-1,5
Grecia	1,80	4,5
Irlanda	1,77	6,0
Islanda	1,15	2,1
Italia	**1,90**	**5,0**
Lettonia	1,57	3,8
Lituania	2,41	3,7
Lussemburgo	1,50	6,7
Malta	2,03	-10,0
Norvegia	1,26	1,1
Olanda	0,77	2,6
Polonia	1,39	7,2
Portogallo	1,72	0,1
Rep. Ceca	3,17	0,7
Romania	1,54	11,1
Slovacchia	1,10	-3,1
Slovenia	1,49	0,7
Spagna	1,59	4,6
Ungheria	1,07	3,4
UE/SEE*	**1,61°**	**3,6**

^Data generated by the European Surveillance System (ESAC-Net) and available in EpiPulse-TESSy as of 20 October 2024.
*EU/EEA: population-weighted average consumption based on all data reported for each year.
°Data refer to the most recent extraction as of 20 October 2024 and may therefore differ from those currently displayed on the online ESAC-Net dashboard

***Table 2**. Hospital consumption of systemic antibiotics (DDD per 1,000 inhabitants per day) by EU/EEA country: 2022–2023 comparison^. Source available: https://www.aifa.gov.it/documents/20142/2766777/Rapporto_Antibiotici_2023.pdf*

In 2023, as shown in Figure 11, only 38.1% of hospital antibiotic consumption in Italy was attributed to 'Access' group antibiotics, compared to a European average of 46%, with no significant changes from previous years [22]. This places Italy among the countries with the highest usage of 'Watch' and 'Reserve' antibiotics, alongside Spain, Romania, Greece, and Bulgaria (Figure 11).

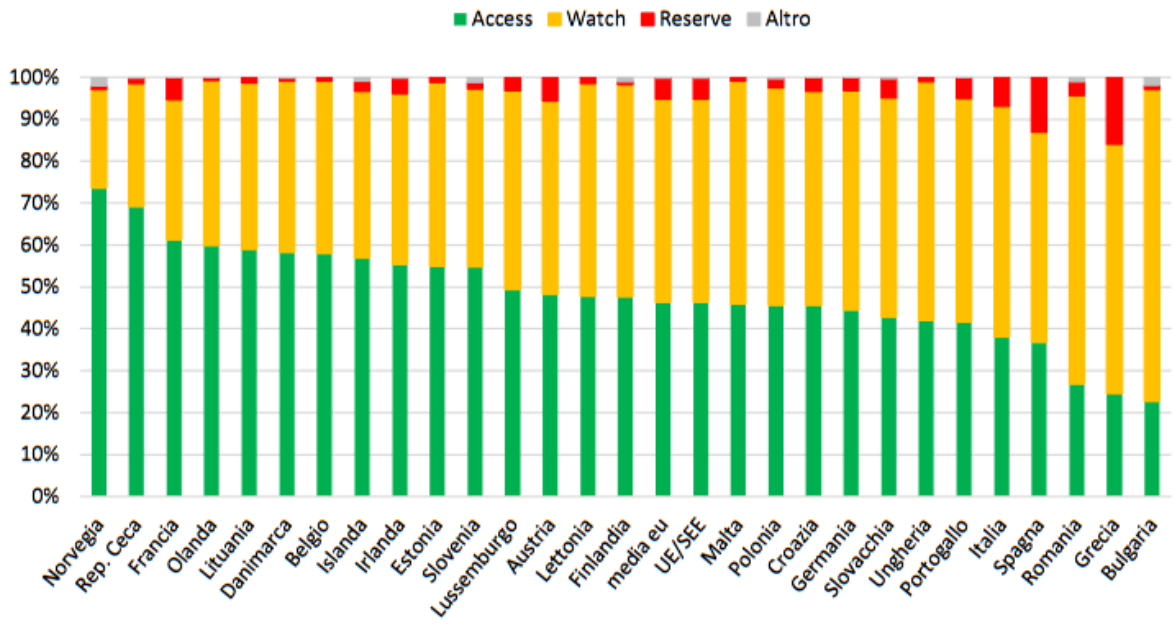

***Figure 11**. Variability by EU/EEA country in hospital consumption (DDD per 1,000 inhabitants per day) of systemic antibiotics (J01) by WHO AWaRe classification in 2023. Source available: https://www.aifa.gov.it/documents/20142/2766777/Rapporto_Antibiotici_2023.pdf*

Italy also reports some of the highest resistance rates in Europe for various pathogen-antibiotic combinations, including macrolide-resistant *Streptococcus pneumoniae*, third-generation cephalosporin-resistant *Escherichia coli* and *Klebsiella pneumoniae*, and fluoroquinolone-resistant *E. coli* and *K. pneumoniae* [22]. Overall, a statistically significant positive correlation exists between increased antibiotic consumption and resistance rates, with Pearson correlation coefficients ranging from 0.67 for *K. pneumoniae* and third-generation cephalosporins to 0.82 for *K. pneumoniae* and fluoroquinolones (Figure 12) [22].

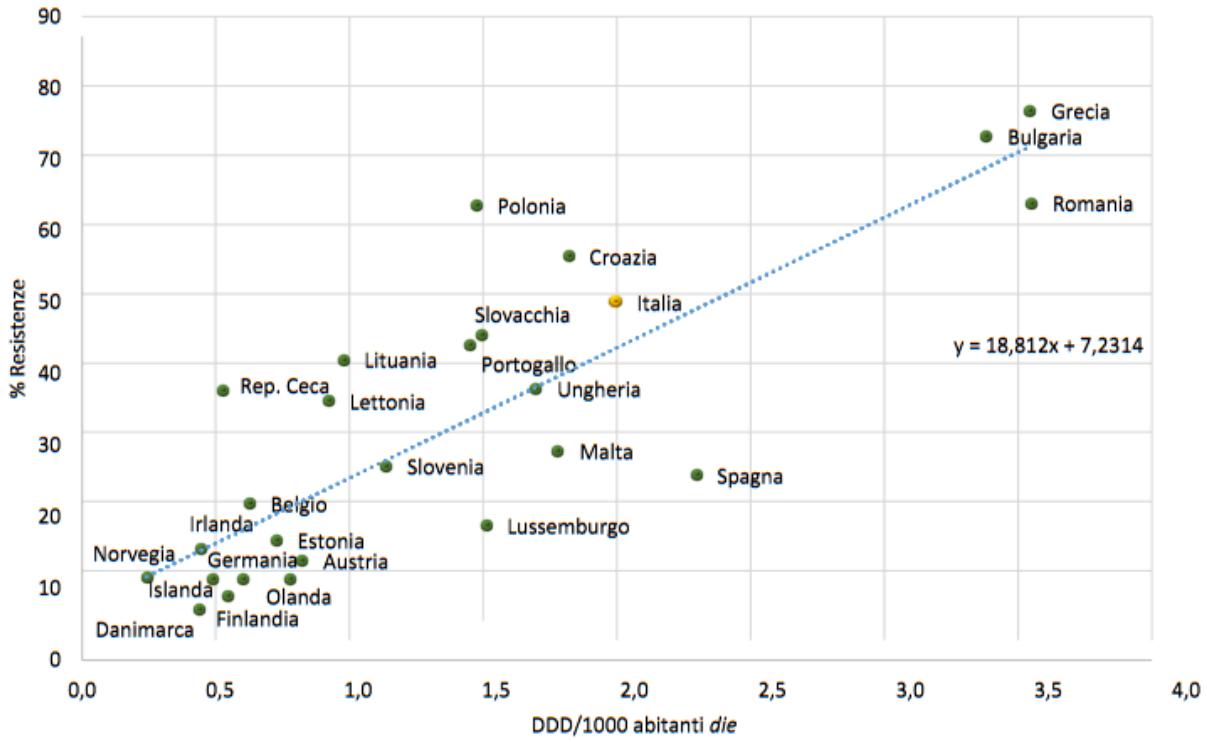

***Figure 12**. Klebsiella pneumoniae: correlation between fluoroquinolone consumption (community and hospital) and resistance percentage by EU/EEA country in 2023. Source available: https://www.aifa.gov.it/documents/20142/2766777/Rapporto_Antibiotici_2023.pdf*

1.1.6 The burden of HCAIs and AMR

The burden of healthcare-associated infections is heavy worldwide, especially due to the high and increasing prevalence of AMR [23], [24], [25], [26]. Patients admitted to hospitals are particularly susceptible to colonisation by and infection with antibiotic-resistant bacteria, due to their frail condition, recent medical procedures, and high level of antibiotic use in healthcare facilities [27], [28]. The WHO estimates that hundreds of millions of patients worldwide are impacted by HCAIs each year, making them the most frequent adverse event during healthcare delivery [1].

HCAIs in Europe lead to more than 90 thousand deaths and corresponding to approximately 2.5 million disability adjusted life years (DALYs), a burden estimated to exceed the cumulative burden of other infections including influenza and tuberculosis in the EU/EEA [6]. DALYs are a time-based measure that combines years of life lost due to premature mortality (YLLs) and years of life lost due to time lived in states of less than full health, or years of healthy life lost

due to disability (YLDs) [29]. One DALY represents the loss of the equivalent of one year of full health: DALYs for a disease or health condition are the sum of the years of life lost to due to premature mortality (YLLs) and the years lived with a disability (YLDs) due to prevalent cases of the disease or health condition in a population [29].

Hospital acquired infections are associated with significant mortality and morbidities: of all HCAIs, central line-associated bloodstream infections and ventilator-associated pneumonias are associated with the highest number of preventable deaths [10]. HCAIs are associated with substantial cost and burden on healthcare organizations: in the United States, it is estimated that HCAIs occur in about two million patients a year with a total number of deaths of 99,000, and cost of $33 billion each year [10].

According to a paperpublished in 2024 by Naghavi et al. [30], in 2021 4.71 million (95% UI 4·23–5·19) deaths were estimated to be associated with bacterial AMR, including 1.14 million (1·00–1·28) deaths attributable to bacterial AMR; it was also estimated that from 1990 to 2021, deaths from AMR decreased by more than 50% among children younger than 5 years yet increased by over 80% for adults 70 years and older [30]. Another analysis published in 2022 by Mestrovic et al. [31] estimated 541 000 deaths (95% UI 370 000–763 000) associated with bacterial AMR and 133 000 deaths (90 100–188 000) attributable to bacterial AMR in the whole WHO European region in 2019.

Resistant infections have a considerable impact on both health and the economy. They are more challenging and costly to treat, often resulting in longer hospital stays and more intense medical care. Moreover, antibiotic-resistant infections have macroeconomic consequences and they are associated with longer sick leave and higher healthcare costs at the individual level, reduce labour supply and labour-force participation, and decrease per-worker productivity, contributing to the Gross Domestic Product (GDP) losses estimated in

macroeconomic models [32]. The latest OECD analysis shows that every year, AMR costs nearly 66 billion United States Dollar at Purchasing Power Parity (USD PPP) across 34 OECD and EU/EEA countries (Figure 13) [13]. The annual cost to the health systems in these countries is estimated to reach around USD PPP 28.9 billion every year and the annual cost to the broader economies is at around USD PPP 36.9 billion [13].

***Figure 13**. The economic impact of AMR. Source available: https://www.oecd.org/en/topics/antimicrobial-resistance.html*

1.1.7 Prevention

HCAIs pose a serious risk to patients, staff and visitors. They can incur significant costs for health systems and cause significant morbidity to those infected. As a result, infection prevention and control (IPC) is a key priority for national and international health agencies, healthcare providers, and other key stakeholders involved in protecting public health[4], [33]. According to the systematic review by Schreiber at al. [34], more than half of HCAIs are preventable, particularly those linked to specific behaviors, through the implementation of structured infection prevention and control programs. However, it is essential to plan and implement these programs at multiple levels (national, regional, and local) to ensure the

application of measures that have been proven effective in minimizing the risk of infectious complications.

Although HCAIs are commonly attributed to patient-related variables and the quality of care provided, evidence suggests that a dedicated organizational structure plays a key role in their prevention. In Italy, for instance, the Hospital Infection Control Committee (HICC) was established to oversee infection surveillance, protocol development, and staff training [2]. Practical measures proven to reduce infection rates include hand hygiene compliance, considered the most effective single intervention to prevent HCAIs; appropriate use of personal protective equipment (PPE); environmental cleaning and disinfection; and safe insertion and maintenance of invasive devices, such as catheters and ventilators [9], [10]. Furthermore, antimicrobial stewardship programs help curb the misuse of antibiotics, thus limiting the spread of resistant organisms like Clostridium difficile and methicillin-resistant Staphylococcus aureus [33]. To prevent HCAIs the role of the interprofessional team is of utmost importance in improving care for patients. The involvement of an interprofessional healthcare team, including infection control specialists, physicians, nurses, and pharmacists, is crucial in delivering coordinated care that prioritizes infection prevention. By following standardized guidelines and engaging in continuous education, healthcare workers can significantly reduce the burden of HCAIs and improve patient outcomes. The ECDC promotes various campaigns to raise awareness of measures for preventing healthcare-associated infections, sharing information including training for healthcare workers and the implementation of proper hygiene practices, which are also highlighted on its website (Figure 14).

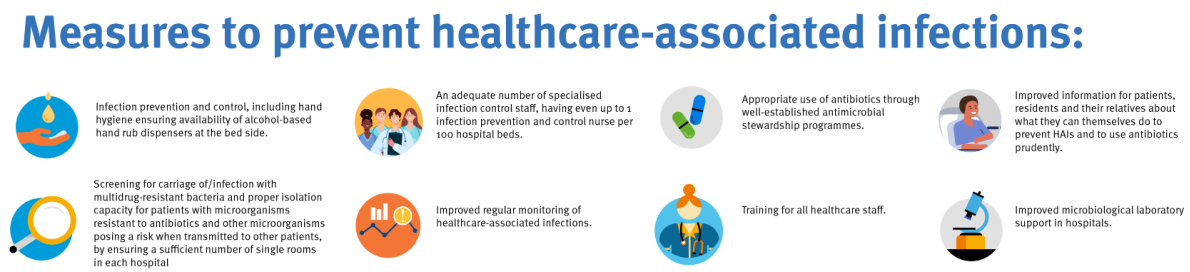

***Figure 14**. Measures to prevent healthcare-associated infections: https://www.ecdc.europa.eu/en/publications-data/healthcare-associated-infections-threat-patient-safety-europe*

In addition, to enhance public and professional awareness of antimicrobial resistance (AMR) across Europe, the European Antibiotic Awareness Day (EAAD) is held annually around the 18th of November [4]. This initiative, coordinated by the European Centre for Disease Prevention and Control, aims to promote the responsible use of antibiotics and to raise awareness about the growing threat of antibiotic-resistant bacteria through coordinated campaigns, educational events, policy engagement activities, and extensive use of social media platforms. An example of such a campaign can be seen in Figure 15.

***Figure 15**. ECDC social media campaign to promote the responsible use of antibiotics and to raise awareness about the growing threat of antibiotic-resistant bacteria. Source available: https://www.ecdc.europa.eu/en/publications-data/social-media-card-healthcare-associated-infections*

Coordinated global actions to respond to Antimicrobial Resistance

Addressing AMR requires both targeted interventions across human, animal, environmental, and food production sectors, and a coordinated global response using a unified approach known as *One Health* (Figure 16), which emphasizes the interconnectedness of people, animals, and ecosystems [11]: this strategy fosters collaboration among stakeholders to design and implement policies, research, and actions to mitigate AMR.

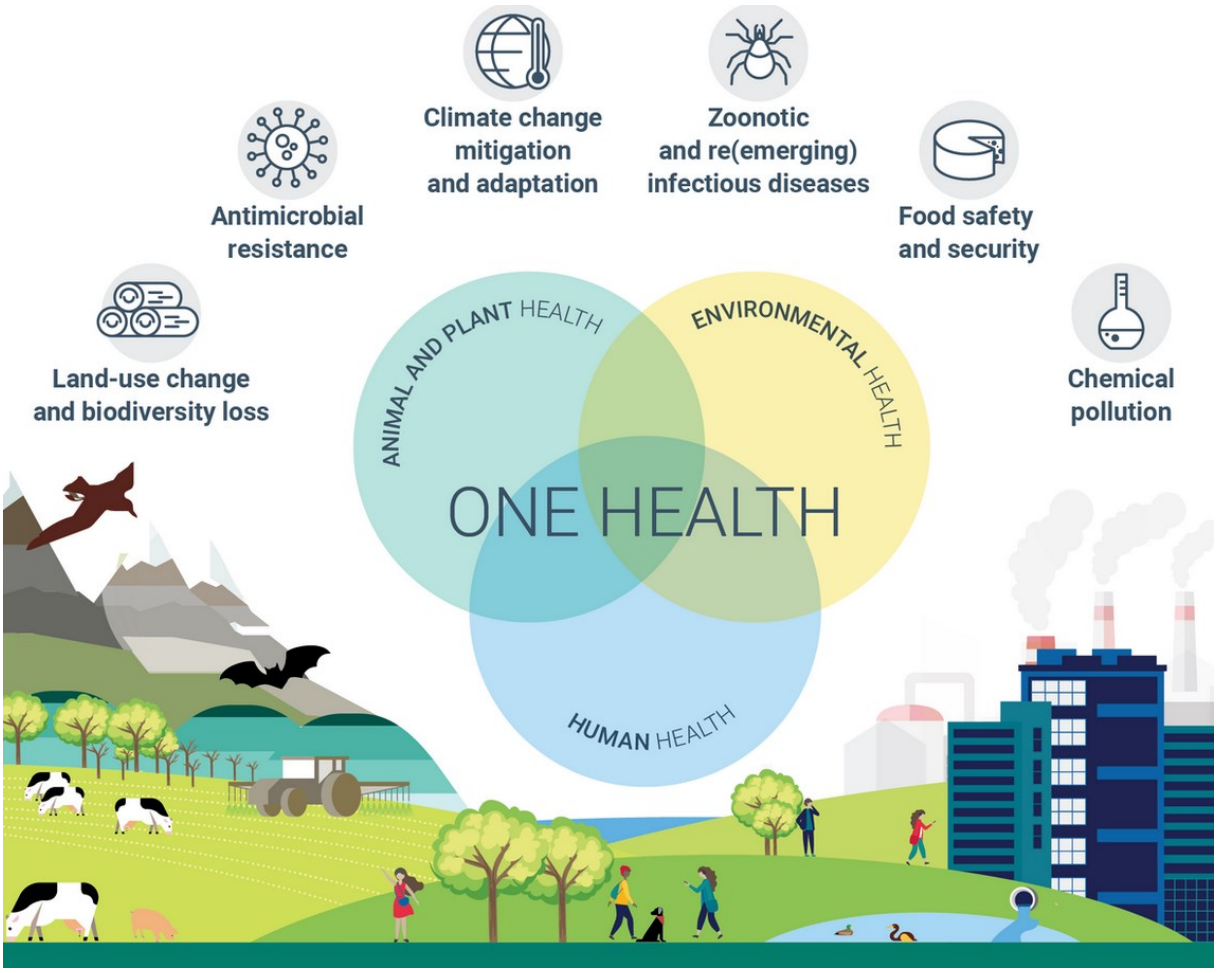

***Figure 16**. Representation of the One Health project. Source available: ECDC: https://www.ecdc.europa.eu/en/one-health*

Return-on-investment (ROI) analysis is a valuable tool for guiding policy decisions. By quantifying the costs and potential returns associated with various policy interventions, ROI analysis can support policy makers in efforts to allocate limited resources to policies that promise the highest return. The latest OECD analysis calculated the ROI associated with 11 interventions and three policy packages: for example, the annual average cost of implementing a One Health package to prevent AMR – involving action in human health and the food sector – is around five times lower than the savings in health expenditure and gains in productivity combined (Figure 17) [13].

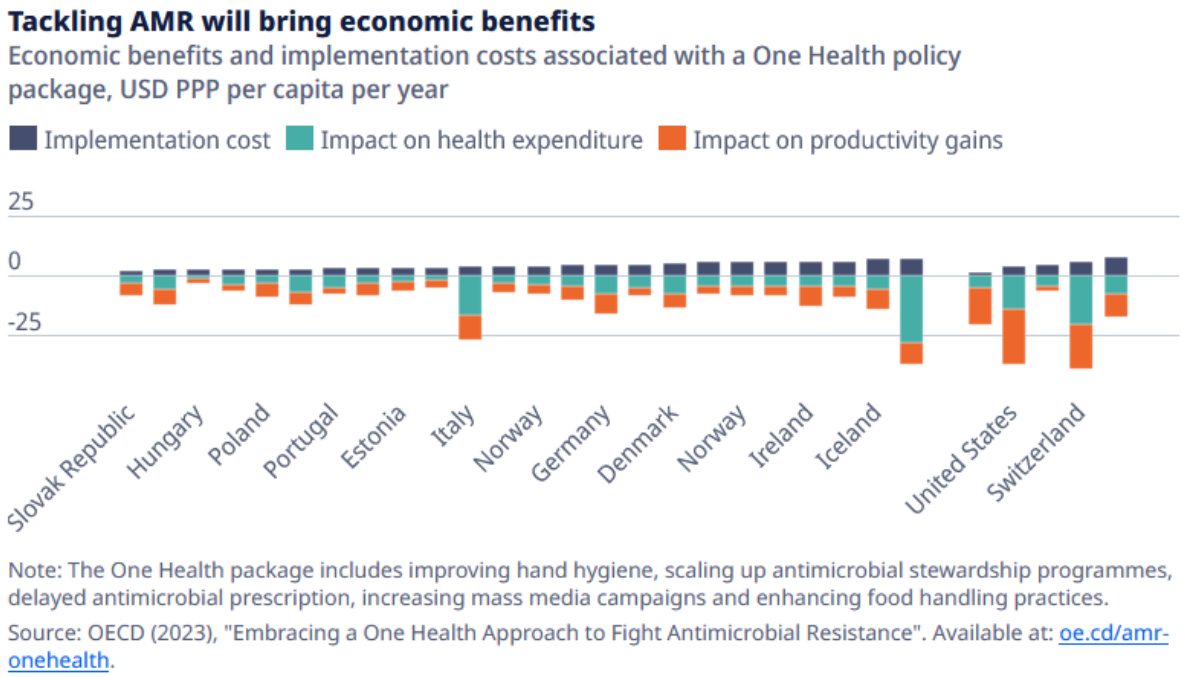

***Figure 17**. Economic benefits and implementation costs associated with a One Health policy package. Source available: https://www.oecd.org/en/topics/antimicrobial-resistance.html*

In 2015, the Global Action Plan (GAP) on AMR was adopted, promoting national action plans grounded in the One Health approach: WHO, together with Food and Agriculture Organization of the United Nations (FAO), United Nations Environment Programme (UNEP) and World Organisation for Animal Health (WOAH) (the Quadripartite"), coordinates global efforts through a joint secretariat, which also supports initiatives like the Global Leaders Group and Multi-Stakeholder Partnership Platform [11]. Several high-level meetings, including ministerial conferences and United Nations (UN) sessions, have helped shape ambitious targets and foster international collaboration [11].

World AMR Awareness Week (WAAW), held annually in November, aims to increase public and policy-level awareness of AMR and best practices.

WHO also promotes a people-centred approach, integrating AMR strategies into broader health systems and universal health coverage: core interventions include infection prevention, accurate diagnostics, and access to appropriate treatment [11].

Antimicrobial stewardship programs, supported by WHO, guide healthcare workers in the responsible use of antibiotics: the AWaRe classification system helps improve prescribing practices by categorizing antibiotics based on their appropriate use [11].

To inform AMR strategies, WHO established a Global Antimicrobial Resistance and Use Surveillance System (GLASS), a global surveillance system that collects data on antimicrobial resistance and usage across sectors [11].

Given the slow development of new antibiotics and limited access to existing ones, WHO supports priority-setting for research and innovation, collaborating with global partners to promote Research & Development on antimicrobials, diagnostics, and vaccines [11]. A list of priority pathogens and key research areas guides these efforts, aiming to ensure access to effective treatments worldwide.

1.2 Hospital networks

Hospitals do not function in isolation; rather, they are embedded in a broader system of interdependent relationships. These institutions are connected to the general population through both patients and healthcare personnel, and they are also interlinked with one another via shared patients who are transferred between facilities. Collectively, these interactions form a complex and dynamic national healthcare network that plays a significant role in the epidemiology of infectious diseases, including antimibiotic-resistant bacteria.

A growing body of research has emphasized the epidemiological importance of patient flow across hospitals in shaping the dissemination of ARB at the national level [35], [36], [37], [38]. For example, Donker et al. demonstrated that patient-sharing networks among hospitals significantly influence the spread of resistant organisms, such as MRSA, in England [35]. Similarly, Lee et al. highlighted how the structure of healthcare networks can amplify or suppress the propagation of ARB depending on the frequency and direction of patient transfers [35], [36], [37], [38].

Intra-hospital networks

Within individual hospitals, a similar networked structure exists at a smaller scale. Hospital wards are interconnected through patient transfers, which facilitate internal mobility and, inadvertently, the transmission of ARB. These intra-hospital networks, shaped by patient movements, form temporal contact structures that are crucial for understanding the micro-dynamics of ARB spread within healthcare settings.

However, these intra-hospital transfer patterns are not static. External shocks or systemic changes, such as those imposed by public health emergencies, can significantly alter the underlying structure of these networks. For instance, the COVID-19 pandemic represented one of the most substantial disruptions to healthcare systems in recent history. In response to rising admissions of critically ill patients, many hospitals suspended elective surgeries and repurposed wards to expand intensive care capacity. These operational shifts likely altered usual patient flow pathways within hospitals, leading to modified contact patterns between wards. As a result, the transmission dynamics of ARB during and after the pandemic may have deviated significantly from pre-pandemic norms, necessitating updated models and surveillance strategies.

Understanding how such structural and temporal variations in healthcare networks, both inter- and intra-institutional, affect the spread of ARB is essential for designing effective infection prevention and control policies. Integrating network science with epidemiological surveillance offers a powerful framework for identifying high-risk transmission pathways and for implementing targeted.

1.3 SARS-CoV-2 pandemic and spread of antibiotic-resistant bacteria

In December 2019, an outbreak of pneumonia of unknown origin was reported in Wuhan, Hubei Province, China. Early cases were epidemiologically linked to the Huanan Seafood Wholesale Market; however, subsequent investigations demonstrated that sustained human-to-human transmission was already occurring before the closure of the market [39]. The causative agent was soon identified as a novel respiratory virus. Genomic sequencing revealed that it belonged to the coronavirus family and was closely related to the severe acute respiratory syndrome coronavirus (SARS-CoV) identified in 2003 (Figure 18) [39], [40]. Consequently, the pathogen was named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a betacoronavirus belonging to the subgenus *Sarbecovirus* [40].

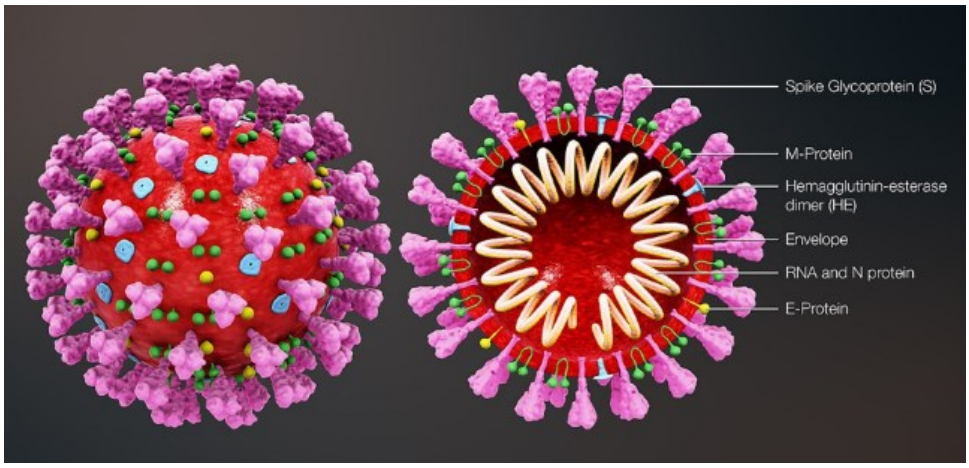

Figure 18. *SARS-CoV-2 representation. Source available: https://www.scientificanimations.com/wiki-images/ and https://www.unisr.it/news/2020/3/viaggio-al-centro-del-virus-come-e-fatto-sars-cov-2*

The rapid dissemination of SARS-CoV-2 across continents, facilitated by global air travel and asymptomatic carriers, together with mounting mortality, prompted the World Health Organization to declare a global pandemic on 11 March 2020 [39], [41]. The disease caused by the virus was officially termed Coronavirus Disease 2019 (COVID-19).

Clinical manifestations of COVID-19 range from asymptomatic or mild upper respiratory tract symptoms to severe pneumonia, acute respiratory distress syndrome (ARDS), multiorgan failure, and death [42]. Common symptoms included fever, cough, fatigue, anosmia, and dyspnea [42]. At the beginning of the outbreak, specific antiviral therapies were not available. Empirical treatments frequently involved the use of antibiotics, corticosteroids, and other supportive measures, despite limited evidence for their efficacy [43].

To curb transmission, governments worldwide implemented unprecedented public health measures, including large-scale lockdowns, physical distancing mandates, mask wearing, travel restrictions, and widespread diagnostic testing; these interventions, although effective in reducing viral spread, carried profound societal costs [44].

A decisive turning point in the pandemic response was the rapid development of vaccines. Within less than a year, several vaccines based on different platforms (mRNA, adenoviral vectors, inactivated viruses, protein subunits) demonstrated high efficacy in preventing symptomatic infection and severe disease. Mass immunization campaigns significantly reduced morbidity and mortality [45].

Beyond its immediate health effects, COVID-19 generated far-reaching consequences across multiple dimensions. Hospitals faced unprecedented pressure, with shortages of intensive care beds, ventilators, and personal protective equipment; the diversion of resources to

COVID-19 care disrupted essential services for other conditions, including cancer, cardiovascular disease, and mental health care [46]. Global Gross Domestic Product contracted sharply in 2020 due to lockdowns and disrupted supply chains; the International Monetary Fund reported the deepest peacetime recession since the Great Depression, with disproportionate effects on low-income populations and vulnerable workers [47]. School closures affected more than 1.5 billion learners worldwide, accelerating reliance on digital platforms and exacerbating inequalities in access to education [48]. Social isolation and uncertainty contributed to a significant rise in anxiety, depression, and other mental health disorders [49].

COVID-19 has proven to be not only a biomedical challenge but also a complex societal crisis, exposing vulnerabilities in health systems, economies, and social structures worldwide. The pandemic highlighted the necessity of global solidarity, transparent communication, and investments in pandemic preparedness.

While intensified infection prevention and control measures implemented in response to the SARS-CoV-2 pandemic have, in some instances, led to a reduction in the transmission of ARB [50], [51], the overall impact of the pandemic on ARB prevalence within hospitals is complex and multifaceted. Enhanced hygiene protocols—such as improved hand hygiene compliance, increased use of personal protective equipment, stricter visitor policies, and environmental cleaning—have likely contributed to limiting nosocomial transmission of various pathogens, including ARB, particularly during the early phases of the pandemic when vigilance was heightened.

However, these potential benefits may have been offset by several concurrent challenges. First, hospitals worldwide experienced substantial disorganisation due to the sudden influx of

COVID-19 patients, leading to the reallocation of resources, staff shortages, and the repurposing of wards. These disruptions may have weakened routine infection control practices, particularly in non-COVID units, where infection prevention and control oversight and staffing may have been deprioritized; moreover, the frequent movement of healthcare workers between wards, the use of temporary or redeployed staff unfamiliar with IPC protocols, and the breakdown in standard cohorting procedures may have inadvertently facilitated the intra-hospital spread of ARB [52], [53], [54]. Another critical factor contributing to the potential rise in ARB during the pandemic is the increased and often empirical use of broad-spectrum antimicrobials in COVID-19 patients. Early in the pandemic, due to the diagnostic uncertainty and concerns about bacterial co-infections, antibiotics were frequently prescribed [55], even in the absence of confirmed bacterial infection. Several studies reported that a significant proportion of hospitalized COVID-19 patients received antibiotics despite relatively low rates of confirmed secondary bacterial infections [56], [57]. This overuse of antimicrobials not only heightened selection pressure for resistant organisms but may have also disrupted patients' microbiota, increasing their susceptibility to colonization and infection with ARB.

Therefore, while the pandemic introduced some IPC improvements, it also created ideal conditions for the emergence and persistence of nosocomial ARB. Understanding these opposing effects is crucial for accurately interpreting ARB trends observed during the pandemic years and for strengthening future outbreak preparedness plans that safeguard antimicrobial stewardship and infection control simultaneously.

2. Aim and study population

In this doctoral dissertation we study the change in the intra-hospital transfer network of the Universitätsklinikum Freiburg (UKF), Germany, and of the Grande Ospedale Metropolitano Niguarda of Milan (GOMN), Italy, between 2019 and 2023, by creating a time-sliced temporal network and simulating the spread of ARB among wards, using the HospitalNetwork R package. This package standardises the data cleaning and network reconstruction process, and was previously used in the other studies, for instance to predicted the time span needed to spread a new pathogen in a given hospital network [58] or to show the correlation between hospital transfer networks and the prevalence of MRSA bacteraemias [35]. Goal of this study is to assess the impact of the SARS-CoV-2 pandemic on the intra-hospital network of a large German university hospital and an Italian univeristy hospital.

2.1 Carachteristics of the hospitals involved

Universitätsklinikum Freiburg – Germany

The University Medical Center Freiburg is a hospital located in Freiburg im Breisgau, Germany (Figure 19).

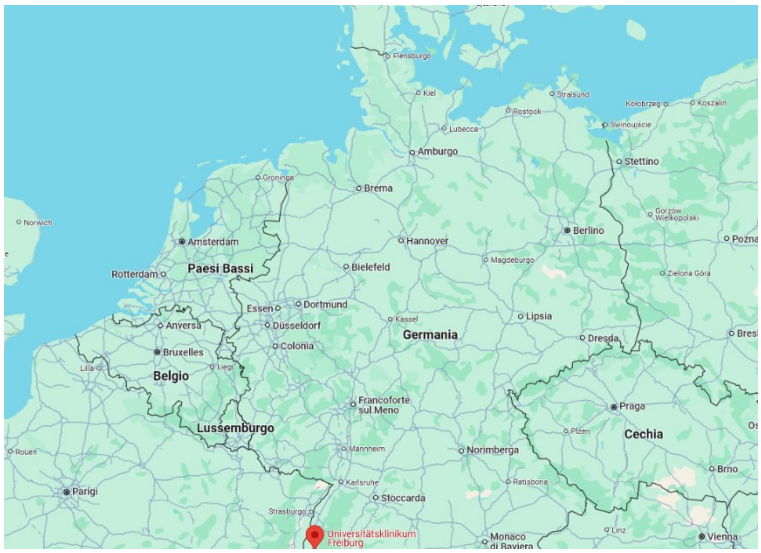

***Figure 19**. Geographic location of Freiburg in Breisgau, Germany. Source available: https://www.google.com/maps*

It is one of the largest hospitals in Germany, based on the number of employed physicians and beds, and is affiliated with the Albert Ludwig University of Freiburg, founded in 1457. According to 2023 statistics, it handled 89,438 inpatient cases, 950,646

outpatient visits, and has 2,179 beds and 15,127 staff members, including 1,904 physicians and 4,444 nursing professionals [59].

The University Medical Center Freiburg is spread across four locations [60]:

- The central hospital is located on the edge of the Stühlinger district in the western part of the city.
- The external clinics for psychiatry, child and adolescent psychiatry, psychosomatics, and dermatology are located on Hauptstraße in the northern district of Herdern.
- The medical-theoretical institutes (anatomy, biochemistry, physiology, forensic medicine) are housed in the university's institute quarter in the Neuburg district.
- Part of the Heart Center as well as the Obesity Center are located on the Bad Krozingen campus at Südring 15.

It comprises 33 clinics and 23 institutes [60]. The Clinics are [60]:

- Clinic for Anesthesiology and Intensive Care Medicine
- Clinic for Ophthalmology
- Department of Surgery
    - Clinic for General and Visceral Surgery
    - Clinic for Thoracic Surgery
    - Clinic for Urology
    - Clinic for Plastic and Hand Surgery
    - Clinic for Orthopedics and Trauma Surgery
    - Clinic for Cardiac and Vascular Surgery (University Heart Center Freiburg–Bad Krozingen)

- Clinic for Dermatology and Venereology
- Clinic for Otorhinolaryngology (Ear, Nose and Throat)
- Clinic for Gynecology
- Department of Internal Medicine
    - Clinic for Internal Medicine I: Hematology, Oncology, and Stem Cell Transplantation
    - Clinic for Internal Medicine II: Gastroenterology, Hepatology, Endocrinology, and Infectious Diseases
    - Clinic for Internal Medicine IV: Nephrology and General Medicine
    - Clinic for Pulmonology
    - Clinic for Rheumatology and Clinical Immunology
    - Clinic for Palliative Medicine
    - Clinic for Cardiology and Angiology (University Heart Center Freiburg–Bad Krozingen)
- Center for Pediatrics and Adolescent Medicine
    - Clinic for General Pediatrics and Adolescent Medicine
    - Clinic for Neuropediatrics and Neuromuscular Disorders
    - Clinic for Pediatric Hematology and Oncology
- Neuroscience Center
    - Clinic for Neurosurgery
    - Clinic for Neurology and Neurophysiology
    - Clinic for Neuroradiology
- Department of Mental Health
    - Clinic for Psychiatry and Psychotherapy

    - Clinic for Psychosomatic Medicine and Psychotherapy
    - Clinic for Child and Adolescent Psychiatry, Psychotherapy and Psychosomatics
- Radiological Diagnostics and Therapy
    - Clinic for Diagnostic and Interventional Radiology
    - Clinic for Radiation Therapy
    - Clinic for Nuclear Medicine
    - Clinic for Neuroradiology
- Department of the University Heart Center
    - Clinic for Cardiac and Vascular Surgery
    - Clinic for Cardiology and Angiology
    - Clinic for Congenital Heart Defects and Pediatric Cardiology
- Department of Dentistry, Oral and Maxillofacial Medicine
    - Clinic for Conservative Dentistry and Periodontology
    - Clinic for Prosthodontics
    - Clinic for Oral and Maxillofacial Surgery
    - Clinic for Orthodontics

Grande Ospedale Metropolitano Niguarda, Milan – Italy

***Figure 20**. Geographic location of Milan, Italy. Source available: https://www.google.com/maps*

The Grande Ospedale Metropolitano Niguarda, formerly known as Ospedale Niguarda Ca' Granda until 2017 and commonly referred to as Ospedale Niguarda, is a historic hospital in Milan, Italy (Figure 20), established in 1939. It is part of the Regional Health Service of Lombardy and currently operates as a Territorial Social and Health Agency (Azienda Socio Sanitaria Territoriale - ASST).

Its healthcare departments include [61]:

- Multispecialty Medical Department
- Cardiothoracic and Vascular Department
- Multispecialty Surgical Department
- Advanced Diagnostic and Therapeutic Technologies Department
- Hematology, Oncology, and Molecular Medicine Department
- Laboratory Medicine Department
- Maternal and Child Health Department
- Neuroscience Department
- Emergency and Urgent Care Department (EAS)
- Mental Health Department

Niguarda also features:

- 4 multidisciplinary centers: Cancer Center, De Gasperis Cardio Center, Transplant Center, and Trauma Center
- An emergency department with a trauma team and air ambulance service
- A skin bank
- A major burn center
- A spinal unit
- A hyperbaric medicine center
- An equine rehabilitation center
- A poison control center
- A dental and stomatology center

It also serves as a university hospital, has approximately 4100 people working there including about 750 physicians and 2000 nurses, 1167 beds, 42 operating rooms and 285 outpatient clinics [61].

3. Methods

3.1 Network analysis: core concepts

Network analysis provides a powerful framework in public health for modelling and understanding how relational structures (contacts, transfers, or other forms of linkage) contribute to the spread of infections, information, or resistances. Network visualisations are frequently described as “maps” since they illustrate the ways in which the actors within a network are interconnected.

At its core, network analysis views a system as composed of partners or nodes (e.g. patients, wards, hospitals, healthcare workers) and edges or links (contacts, transfers, interactions) as shown in Figure 21, whose patterns give rise to pathway dynamics rather than treating individuals in isolation [62], [63].

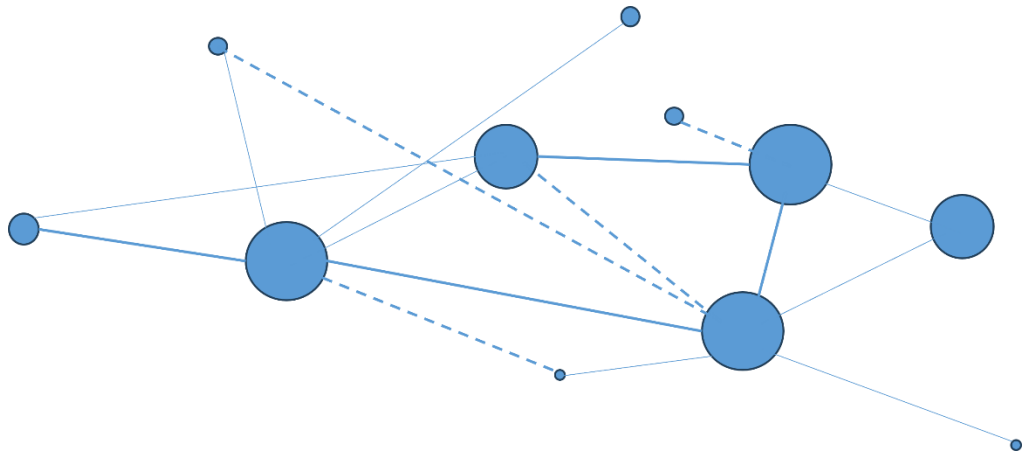

Figure 21. *Depiction of a network, with nodes and links.*

Nodes are represented in network maps as a shape, typically drawn as circles or squares. To convey additional information, nodes can be distinguished by shape or colour. Their size is not fixed: it can be scaled in relation to structural features such as the number of direct connections a node has, or its strategic role in linking partners together [62]. In this way, the map encodes not only who is present in the network, but also their relative position and influence.

Links are usually represented as lines between partners and indicate that they are connected in some way. These connections can take a variety of forms. First, they can be represented as directed or non-directed (link characteristic: direction) as in Figure 22; the directed ones are usually depicted with an arrow indicating that something goes *from* one partner *to* another.

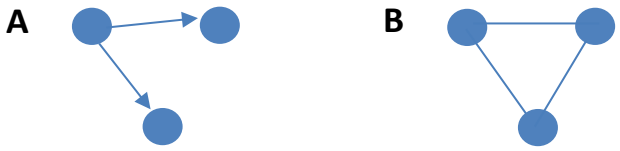

***Figure 22**. Link charachteristics: panel A) directed connections, panel B) non-directed connections.*

Moreover, the connections can be weighted or non-weighted. The strength of a relationship can be rated on a scale, such as how strong it is (in hospital networks, a strong relations means a lot of patients are shared between the nodes); this is usually displayed playing with the thickness of the lines, where thicker lines mean stronger links (Figure 23). Non-weighted connections are represented as simple lines and indicate a "binary" connection: either it is present or not.

***Figure 23.** Link charachteristics: weighted connections.*

Network analysis can provide numbers describing each partner in the network. Key node-level descriptive statistics include [62], [64], [65]:

- degree or degree centrality: how many connections a node has (the sum of direct edges each node has). When analysing directed networks, the in-degree is defined as the number of *incoming* connections while the out-degree as the number of *outgoing* connections (Figure 24). For non-directed networks, sizing by degree highlights nodes that can reach many organizations directly.

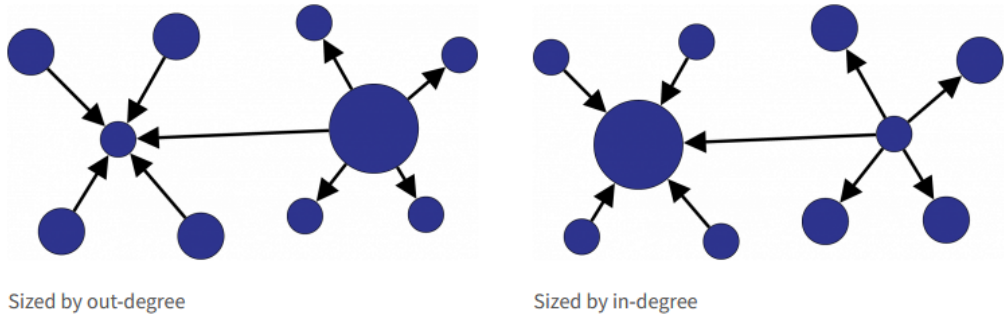

***Figure 24**. Representation of two networks sized, respectively, by out-degree and in-degree. Source available: https://cphss.wustl.edu/methodsandstrategies/social-network-analysis/network-analysis-101/*

In weighted network, instead of only counting if there is an edge or not, also edge weights could be taken into account: this is known as strength centrality (which can also be in-strength and out-strenght).

- betweenness centrality: the extent to which a node connects other nodes that are not otherwise connected. It is defined by calculating how often a node is on the fastest route between two other nodes: the fastest route can be the shortest path (unweighted network) or the shortest path length (weighted network).

  High degree and high betweenness usually coincide, but not always (Figure 25). A node might have a very low degree, but be in a key position so that two nonadjacent (not directly connected) nodes that want to be connected, have to go through that specific node, so it has very high betweenness. Nodes with high betweenness have a great deal of control over exchange in the network and may highlight bottlenecks.

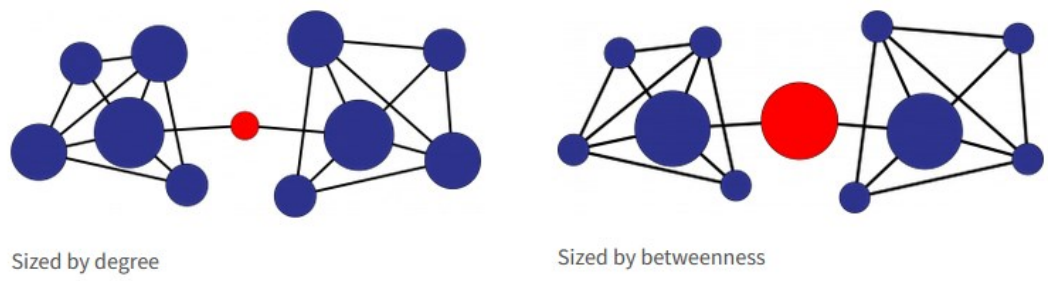

***Figure 25.** Representation of two networks sized, respectively, by degree betweenness. Source available: https://cphss.wustl.edu/methodsandstrategies/social-network-analysis/network-analysis-101/*

- closeness centrality: how edges connect nodes across the whole network is one of the core interests in network science; for studying this, the path length is used. The path length is defined as the number of steps (edges) it takes to get from one node to another. A limitation of degree (and strength) centrality is that only direct ties or path lengths of one are taken into account, though nodes in a network are often indirectly connected, with a path length of two or more. Therefore, a global measure of centrality was introduced and named closeness, taking into account also indirect connections.

- brokerage: is similar to betweenness in that nodes connect otherwise unconnected nodes, with the additional concept of taking the category of nodes into account. Several roles exist, depending on the configuration: coordinators are nodes which connect nodes all from the same category; consultants are nodes which belong to a different category than the nodes they connect, but the unconnected nodes are of the same category; liaisons are nodes that belong to a different category than the nodes they connect , and the unconnected nodes are also from different categories.

  Sizing by coordinator role highlights nodes that can bring together nodes from the same group while sizing by consultant role also highlights nodes that can bring together nodes from the same group, but a group that they themselves are not a part of [62]. Sizing by liaison role highlights nodes that can bring together nodes from different groups that they themselves are also not a part of [62].

In addition to node-level metrics, network analysis can provide numbers that describe the network as a whole [62]:

- average degree: the average number of connections per node.

- density: the proportion (percentage) of all possible links that actually exist. The density and the average degree indicate the level of connectivity in the network.
- centralization: how much the structure is dominated by one or few highly-connected or bridging nodes. Degree Centralization indicates the extent to which the network has one or a few nodes that have a large number of connections. Betweenness Centralization indicates the extent to which the network has one or a few nodes that keep the network connected. Both types of centralization are highest in a "star" type network, where one node is connected to all of the others, but all of the others are only connected to the central node. Centralization is lowest when the network is saturated (all of the nodes are connected to all of the other nodes). "Pendants" are nodes that are connected to the network by only one link while "isolates" are nodes completely disconnected from the network. Highly centralized networks can be very efficient, with a few central nodes able to reach others directly with little redundancy. They can also be sensitive to disconnection; if several nodes are dependent on a single hub and that hub experiences a failure, the dependent nodes will be disconnected from the rest of the network.
- modularity: the extent to which connections happen between the same kinds of nodes more often. Networks with high modularity have more connections between the same types of nodes, networks with low modularity are less siloed (Figure 26). Clusters are distinct subgroups of nodes within the network that are more densely connected to

each other than to nodes outside the group based on a certain chosen metrics.

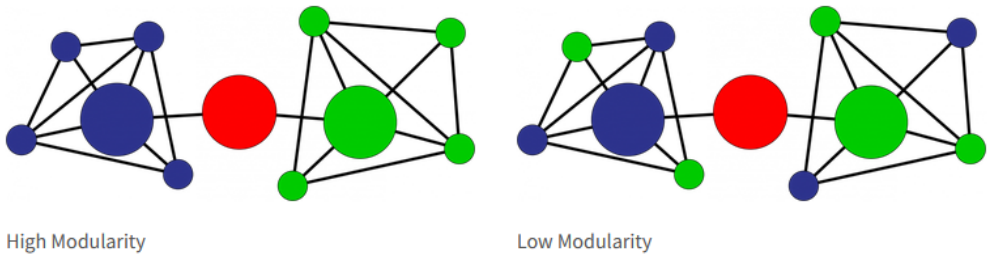

***Figure 26**. Representation of two networks respectively with high and low modularity. Source available: https://cphss.wustl.edu/methodsandstrategies/social-network-analysis/network-analysis-101/*

These measures allow us to characterise connections and, in the end, to understand vulnerability (which nodes or hospitals are likely to act as super-spreaders), robustness (how disease- or resistance-transmission might be contained by disrupting key connections), and to model interventions (for example, isolating or vaccinating high-betweenness nodes). In the context of antibiotic-resistant bacteria, network analysis has been used to map patient transfers among wards or hospitals and detect how hospital-connectedness influence the spread of pathogens.

3.2 General Methodological Framework

In this study we collected detailed admission and discharge data as well as the wards of stay for each patient admitted to the UKF and to the GOMN in the years 2019 until 2023 through clinic databases. We then reconstructed the intra-hospital transfer network, to understand which wards are more connected, and therefore could spread a potential nosocomial pathogen faster.

First, we divided the data into slices for each month, using the admission date as inclusion criterion. This process was repeated for the five-year study period, resulting in a total of 60 slices for UKF. Since the data extraction for GOMN was based on discharge date, to handle censoring in the last part of our complete dataset, we excluded patients being admitted from

the 1st of November 2023 onwards, having checked that 99% of all admissions have ended after circa 40 days. This resulted in a total of 58 slices. We ensured the data was ready for processing using the checkBase function within the HospitalNetwork R package [66]. This function performs various checks, including data consistency, to ensure the database is correctly formatted, and adjusts overlapping patient records.

Following this, we created the network using the HospitalNetwork R package, delivering one network per time slice, 60 networks in total for UKF and 58 for GOMN, including any admission that happened within 30 days after discharge from the previous ward as an inter-ward transfer, to account for the potential risk of ARB reintroduction upon readmission after a stay at home or at another healthcare facility. For each network, we calculated the nodes' in-strength and in-degree as well as the total number of connected wards in the network. The instrength was defined as the number of patients received by a focal ward from the other wards in the network, while the indegree represented the number of wards a focal ward received patients from.

3.3 Simulation

In order to assess the robustness of the intra-hospital network against the spread of ARB in each month, we created a ward-based simulation of potential ARB spread, along the same line as Ciccolini et al. [58]. In short, each ward is considered to be affected by ARB or not, and the probability of a ward getting affected is a function of the total number of received patients from affected wards as well as a transmission scaling parameter c.

$$P_i^{S\to I}(t) = c \sum_{j:H_j=I} w_{ij}\delta t$$

The expression j:Hj=I indicates that the weight should be summed over all wards that have already been affected by the pathogen, and thus have state I. This equation approximates the

actual probability as long as both the summed weight of the incoming connections and the transmission scaling factor c are small, and therefore P<<1. For higher values we should use

$$P_i^{S\to I}(t) = 1 - \prod_{j:H_j=I} (1-c)^{w_{ij}\delta t}$$

which describes the probability of a successful introduction as 1 –the product of the probabilities of the event not happening over each of the connections from affected ward.

For each time step in the simulation, random number generating determined if non-affected wards became affected based on this probability. We assumed wards do not revert to an unaffected state, thus assuming indefinite colonisation of the ward. The probability that a single patient transmits the disease from an affected ward to an unaffected one (i.e. the transmission scaling factor c) was set at 0.001 for UKF and at 0.003 for GOMN. In fact, with a transmission probability of 0.001, for GOMN early saturation was observed in the curve of robustness. Reasons for this are the different patient flow and the difference in wards size between Milan and Freiburg that affect the transmission risk. In fact, the mean ward size in GOMN is smaller: there are many wards with fewer patient transfers between pairs of wards.

Each ward in each month's network was used 25 times as the starting point of the outbreak, resulting in 25 times N model realisations per time slice, with N being the total number of wards in the time slice network. We ran each simulation for 1000 time steps.

We express the robustness of the network as the median time required for the simulated pathogen to reach 25 wards from each of the starting wards. Per starting ward, the time to reach these 25 wards is taken as the median over all 25 simulation runs. We chose a fixed number of wards (i.e. 25) over a percentage (e.g 50% of the wards), as it better captures the speed of spread in differently sized networks. This is important because some wards are

sometimes disconnected from the network, or data are not available, influencing the size of the network. We chose the number of 25 wards to reflect the initial spread of the pathogen, but this is otherwise an arbitrary amount.

The exact value of the measure unit of time for this analysis is arbitrary, since it relates to the transmission parameter, and is meant to give a comparison of robustness amongst months.

To provide a graphical representation of the simulation model, we included an example referring to a single time slice (Figure 27). Fictive values were used due to the impossibility of displaying the actual data within the limited space available. In this example case, the number of wards (N) is six, labelled from A to F, and the time considered to calculate robustness corresponds to the timestep required to reach only three wards (t3).

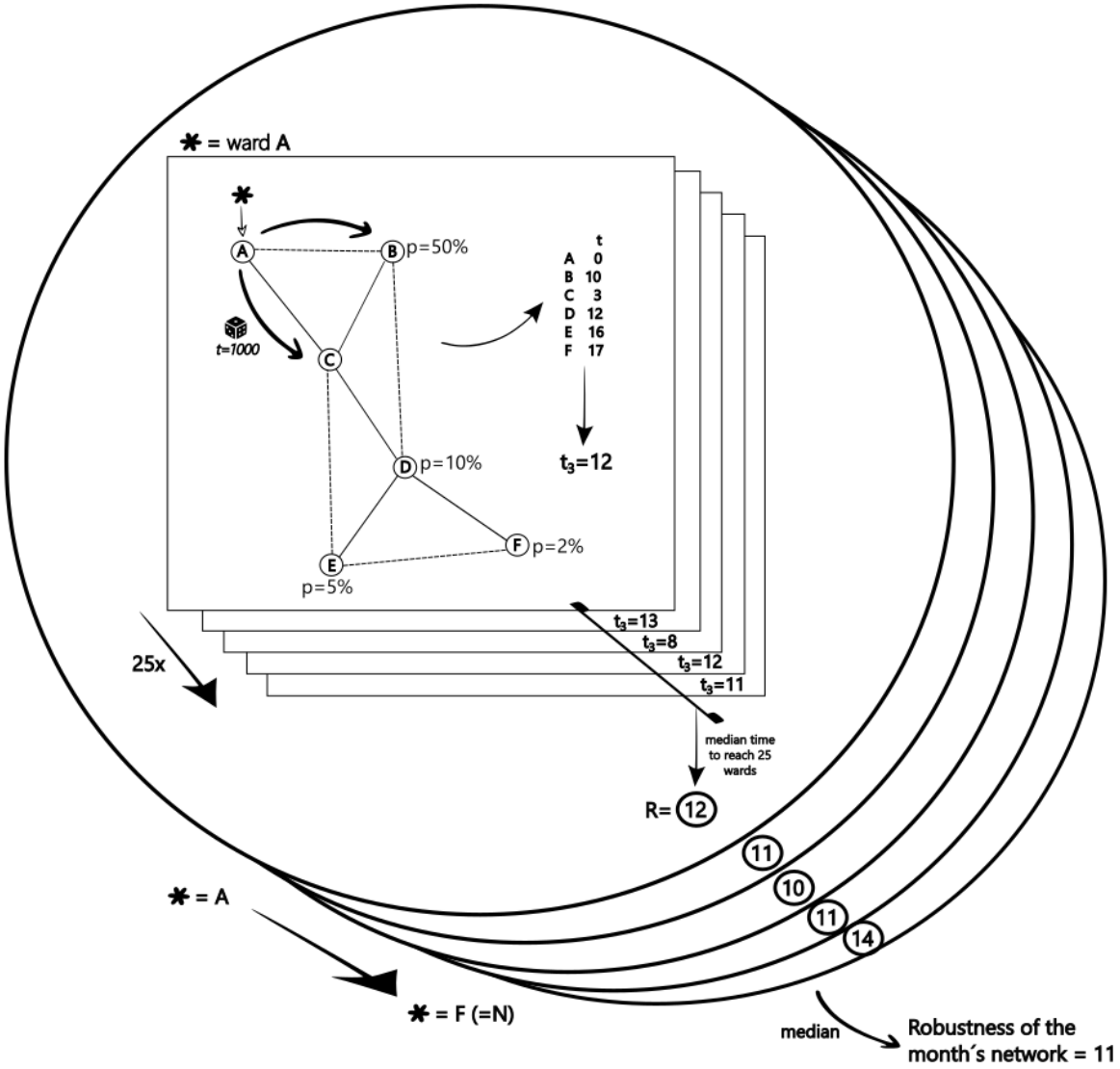

Figure 27*. Graphical representation of the model used for simulating an ARB outbreak with fictive values. N = number of wards; A–F = wards; p = probability; t = timesteps; t3 = timesteps needed to reach three wards; R = robustness.*

We used R version 4.3.2 and the package "HospitalNetwork" to reconstruct the network.

3.4 UKF

The UKF has undergone structural changes by merger with the Universitäts-Herzzentrum Freiburg – Bad Krozingen (UHZ) in April 2021 during the observed period. The number of wards that are interconnected therefore increased, potentially influencing our analysis. The chosen definition of robustness allowed us to compare the values before April 2021 while being less affected by the network size difference.

Being aware of the addition of new wards from April 2021, we identified them and then split the dataset into an original dataset and a dataset excluding the new wards. We defined new wards as any ward that existed in the dataset after June 2021, but did not exist before December 2020. We chose the period from January 2021 until June 2021 as a transition period. We performed the same descriptive statistics and analysis on both datasets.

3.5 GOMN

To understand and estimate what and to which extent can affect the robustness measure, the number of links, the number of transfers and the modularity were calculated per each month. The number of links is the total number of pairs of nodes (in this case wards) that are connected (i.e. where one or more transfers happened between), while the number of transfers gives the total number of transfers that happened between any pair of nodes (wards). Modularity is a measure of the structure of networks: it measures the strength of division of a network into modules or clusters [67]. When modularity is high, the network has dense connections between the nodes within modules but sparse connections between nodes in different modules.

4. Results

4.1 UKF

A total of 236,909 patients were admitted to the UKF during the years 2019 to 2023, with 76,679 of them being admitted to one ward only, and 992,020 patient movements observed during this period. There was a total of 175 unique wards in the UKF during the study period, with the number of wards admitting patients ranging from 110 to 153 per month (Table S 1), of which 98 to 138 were connected in the network.

Within the whole dataset (Table S 1), the number of wards was, on average, 118 until March 2021, and subsequently increased to an average of 143 from April 2021 onwards; the average number of patients until March 2021 was 9,600 while it increased to 12,853 from April 2021. With an increase in patients and wards, the mean indegree and instrength per month were also higher after April 2021: averaging at respectively 5.88 and 7.02 wards before and after April 2021 (indegree), and 36.29 and 44.65 patients (instrength). The mean length of stay per month was relatively homogeneous through the years with an average of 3.40 days. The lowest values in terms of number of patients, of wards, and subsequently lowest measurements of connection can be seen in April 2020.

In order to identify the newly added wards, we labelled all wards present before December 2020 as the original UKF wards, and labelled any wards present from June 2021 that were not original UKF wards as newly added wards. There were 136 original wards, and 39 newly added ones, while 6 wards closed during the transition, resulting in 169 wards after the transition.

In Table S 2, showing the descriptive statistics for the dataset without the newly added wards, we can see more homogeneous values: per month the number of patients ranged from 7139 to 10,839, with a mean of 9783, the number of wards range from 110 to 123 (mean 117), the mean indegree range from 4.40 to 6.66 wards (mean 6.00), the mean instrength ranged from

30.50 to 42.05 patients (mean 37.26), and the mean length of stay ranged from 3.19 to 3.73 (mean 3.44 days).

The comparison between both datasets can be seen in the panels of Figure 28, where the blue lines correspond to the statistics of the complete data set and the red lines to the statistics including only the original UKF wards.

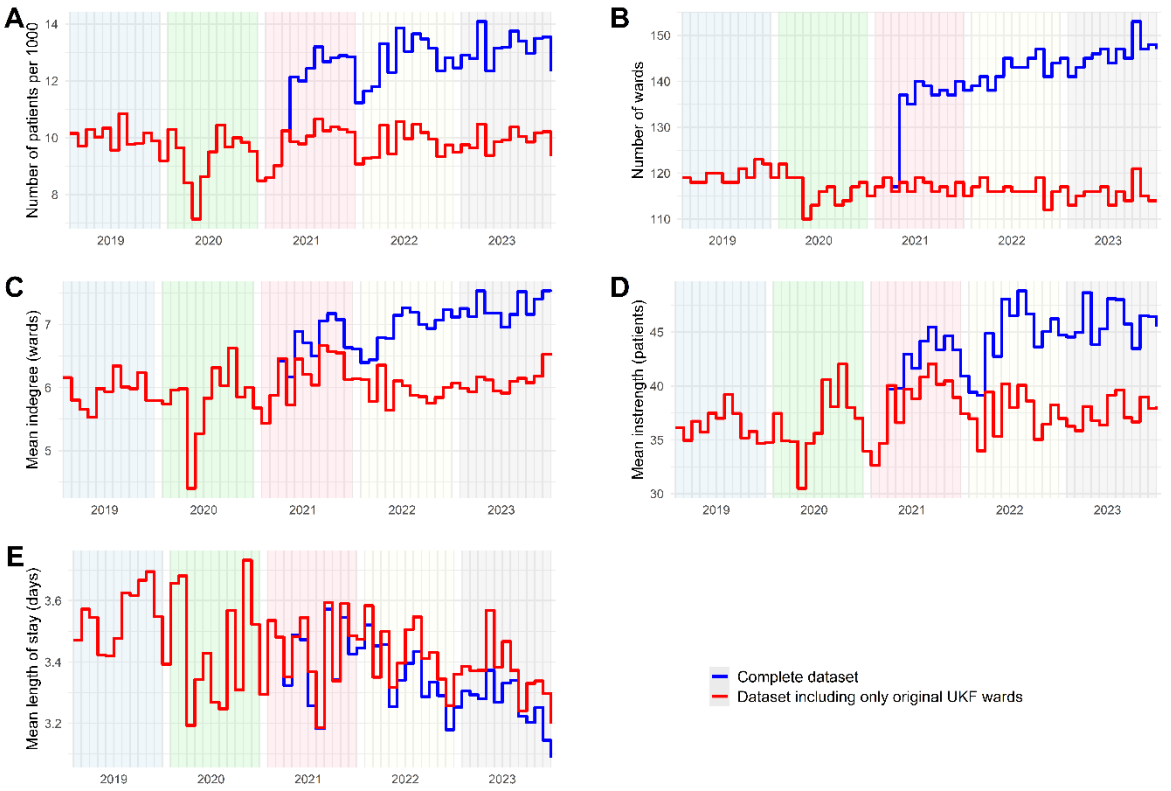

Figure 28. *Descriptive statistics of the complete dataset (blue line) and of the dataset including only the original Universitätsklinikum Freiburg (UKF) wards (red line) showing A) the number of patients, B) the number of wards, C) the mean indegree (wards), D) the mean instrength (patients), E) the mean length of stay (days).*

The total number of wards present in the dataset was 175 however, not all of them were connected to others. In the supplementary Table S 3 we show for each ward in how many months and which it is included, respectively for the dataset including all the wards and for the dataset including only the original wards.

Regarding data including the complete dataset, it can be observed that in April 2020, the network was more robust (t=404) than any of the previous and subsequent months, with a mean respectively of 266 and 228 (Figure 29, blue line).

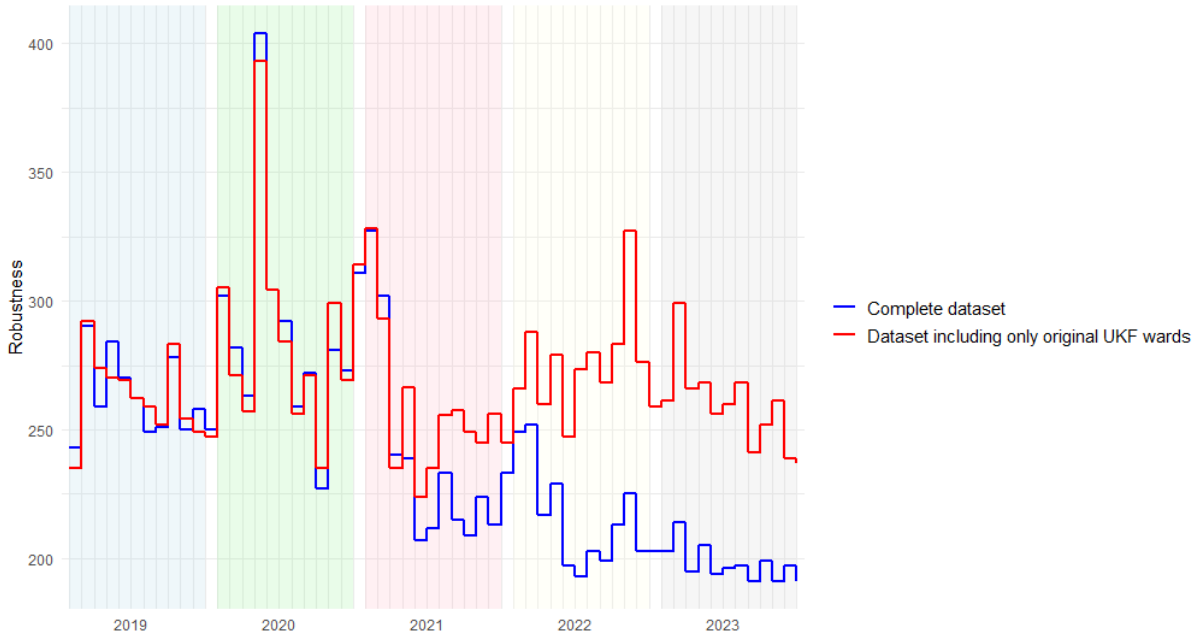

***Figure 29**. Robustness of the intra-hospital network over the study period, with blue line showing data including the complete dataset and red line data including only the original Universitätsklinikum Freiburg (UKF) wards.*

Furthermore, it can be observed that from April 2021 onwards, and more evident from June 2021, robustness was lower than that observed in previous periods, with an average of 210. Other peaks in robustness corresponding to December 2020 and January 2021 with a median of respectively 311 and 327, as well as relative peaks in January and February 2022, are also visible on the graph. The robustness of the network excluding the new wards, shows the same robustness peak in April 2020 (Figure 29, red line), as well as the peaks in December 2020, January 2021, and October 2022. However, the values in the months before and after April 2020 are now similar.

These results are also visible in the mean proportion of wards affected at each time step of the simulation for each year using data including only the original UKF wards, as well as when using the complete dataset, respectively (in Figure 30 and Figure 31).

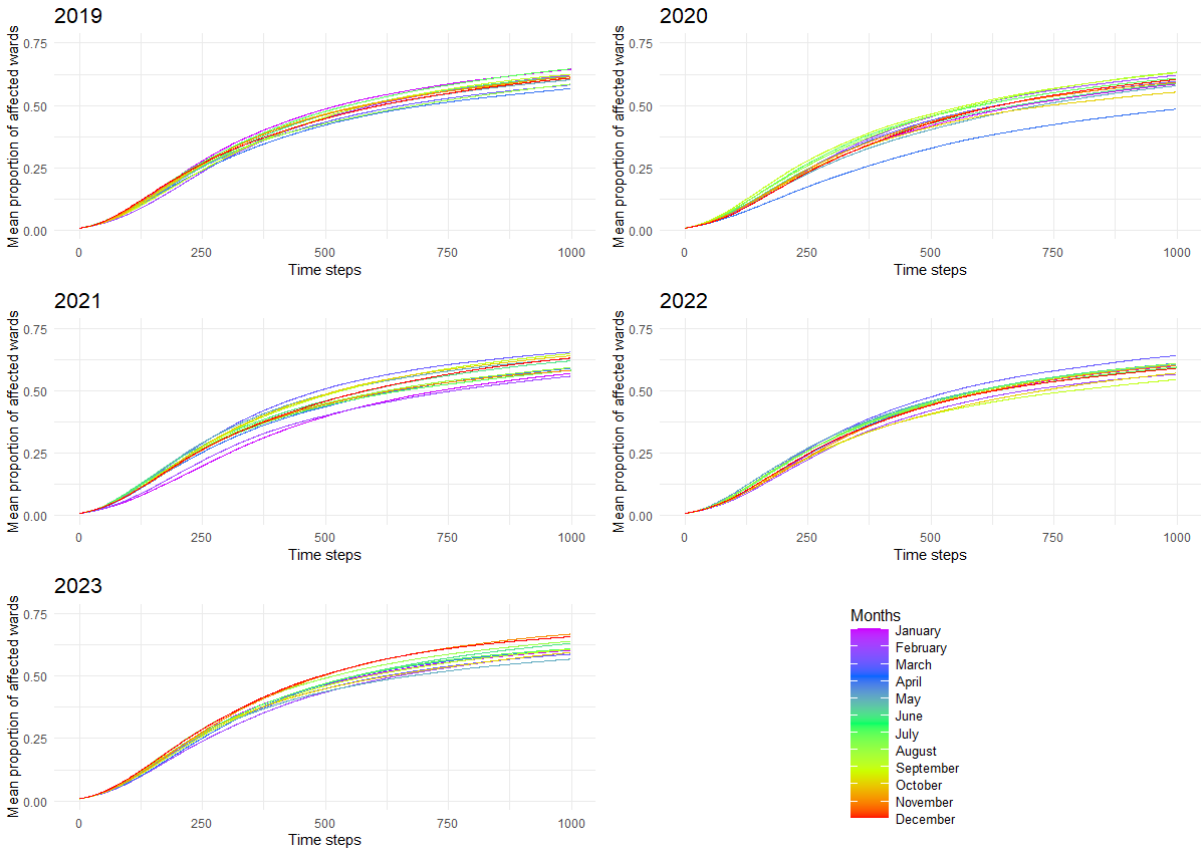

Figure 30. *Mean proportion of wards affected at each time step of the simulation for each year for the dataset, coloured by month, based on the networks including only the original UKF wards.*

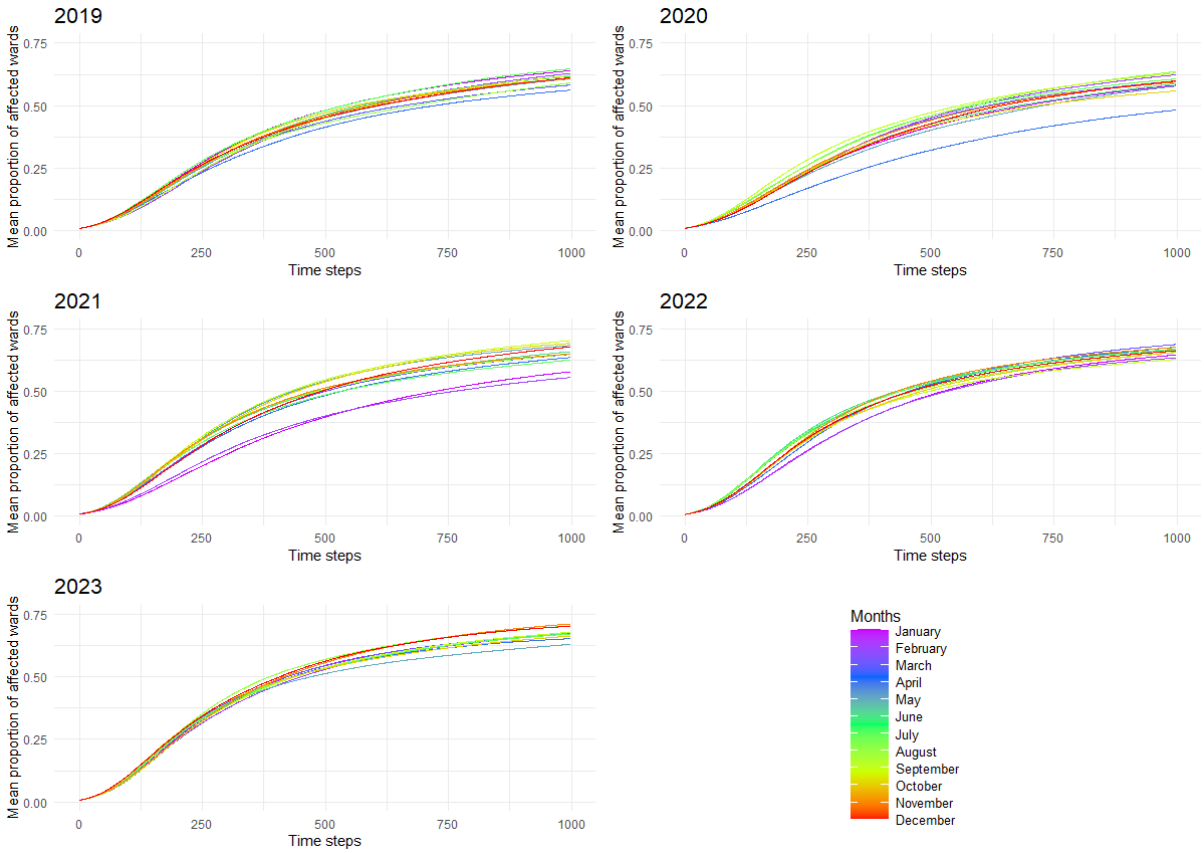

Figure 31. *Mean proportion of wards affected at each time step of the simulation for each year for the whole dataset.*

The lower line in April 2020, indicates that it would take longer for the infection to spread in that month. The other lines are more compact, showing comparable robustness for all months in those years. When comparing the network connectivity during April 2020 with previous months (Figure 32), it can be observed that the reduction in patient movement is happening across most connections, while only a few ward pairs increase their connectivity.

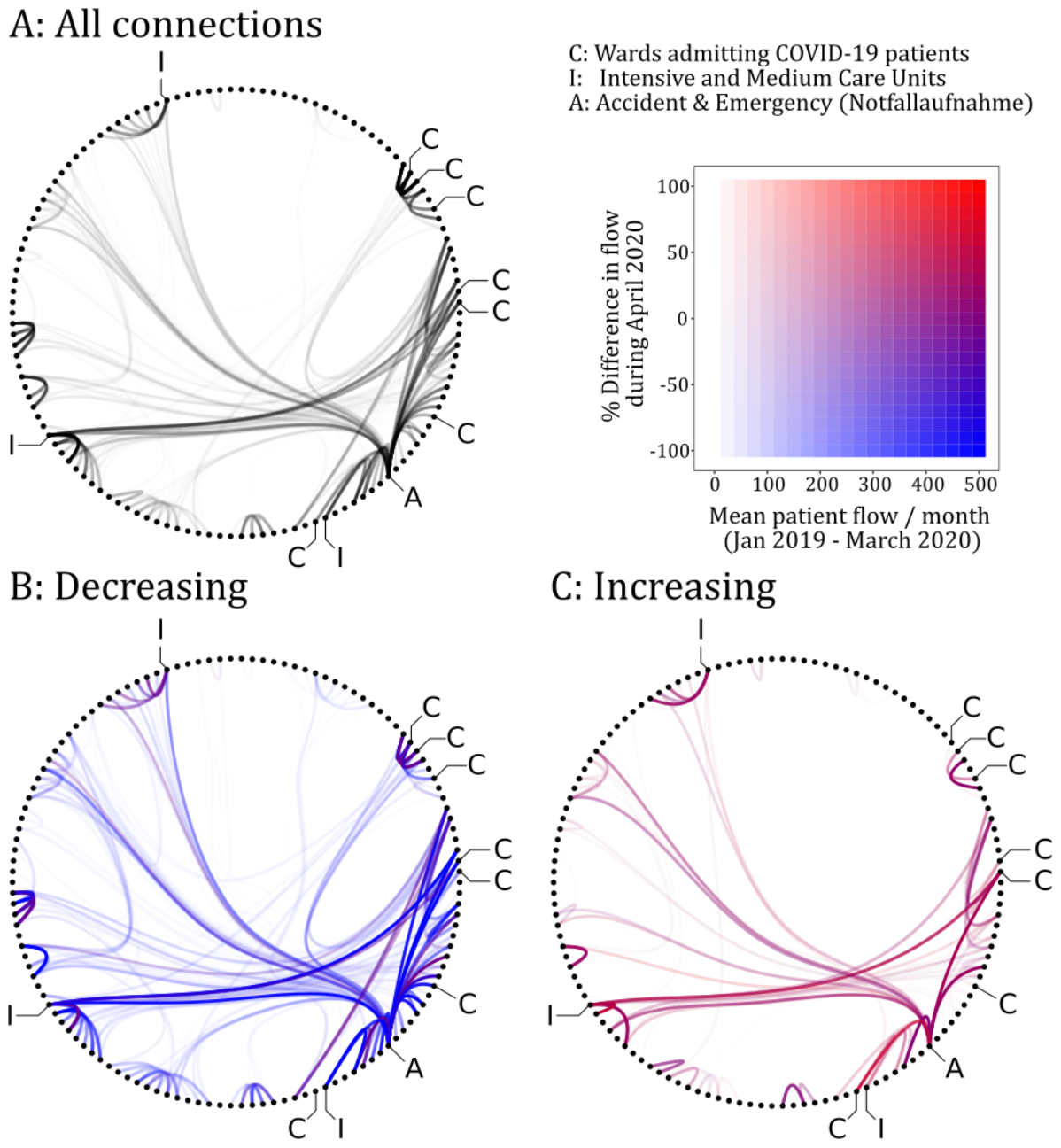

Figure 32. *The change in patient movements in the intra-hospital network of the UKF in April 2020, compared to January 2019 to March 2020. A) The mean network for January 2019 to March 2020, with each dot depicting a ward (with COVID-19 wards, ICUs, and A&E annotated), and connections coloured by the mean number of monthly patient movements between them. B) The decreasing connections, coloured by their reduction, and C) the increasing connections.*

4.2 GOMN

A total of 124,980 unique patients were admitted to the GOMN during the years 2019 to 2023, with 73,715 of them being admitted to one ward only, and 303,637 patient movements observed during this period. There was a total of 252 unique wards in the GOMN during the study period, with the number of wards admitting patients ranging from 100 to 184 per month (Table S 4), of which 75 to 132 were connected in the network.

As shown in Table S 4 and in Figure 33, the number of wards as well as the number of patients through the years (panel A and B) was relatively homogenous over the five years (mean number of wards=148, mean number of patients=4267) but decreased in the months of August every year, in March, and April 2020, while it relatively increased in October 2020. With an increase in patients and wards, the mean indegree and instrength per month (Figure 33, panel C and D) were also higher in October 2020 (respectively 4.22 and 12.08) but also in March 2020 (respectively 4.28 and 11.11) in comparison with the average over study period (respectively 3.37 and 8.38).

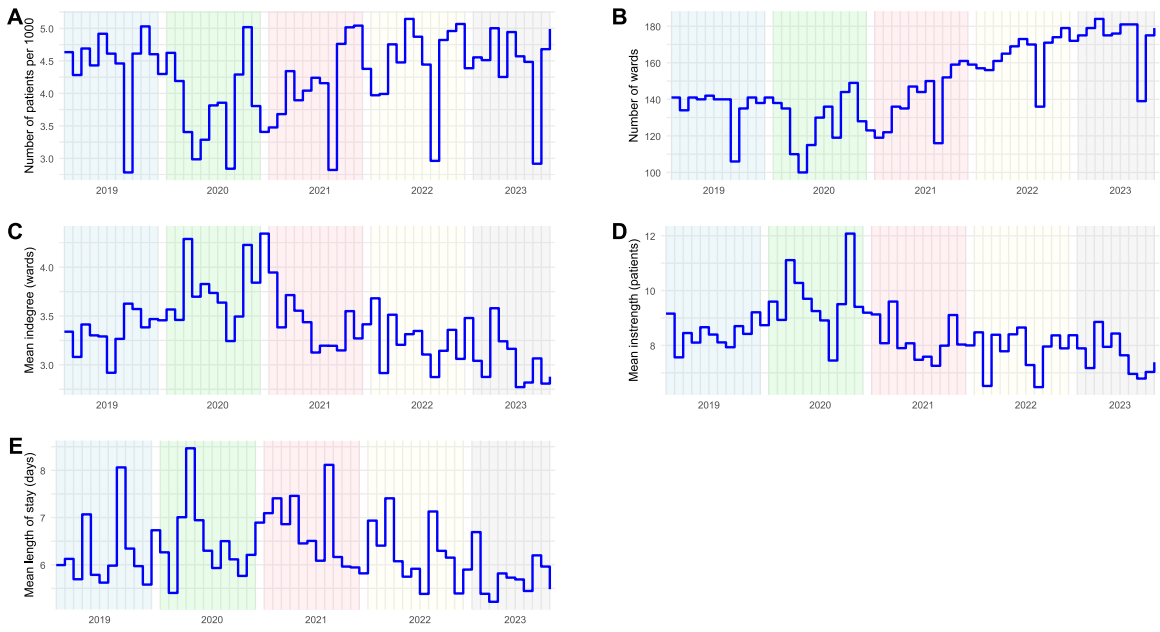

***Figure 33**. Descriptive statistics of the dataset of the Grande Ospedale Metropolitano Niguarda (GOMN) showing A) the number of patients, B) the number of wards, C) the mean indegree (wards), D) the mean instrength (patients), E) the mean length of stay (days).*

The mean length of stay per month was relatively homogeneous through the years, with its peak in April 2020 (8.47 days), as shown in Figure 33, panel E.

The total number of wards present in the dataset was 252 however, not all of them were connected to others. In the supplementary Table S 5 we show for each ward in how many months and which it is included.

Figure 34 shows the number of patient transfers over the study period, which remained relatively high (884) in April 2020, comparable to other months (mean number of transfers=896), and were higher in October 2020 (1377).

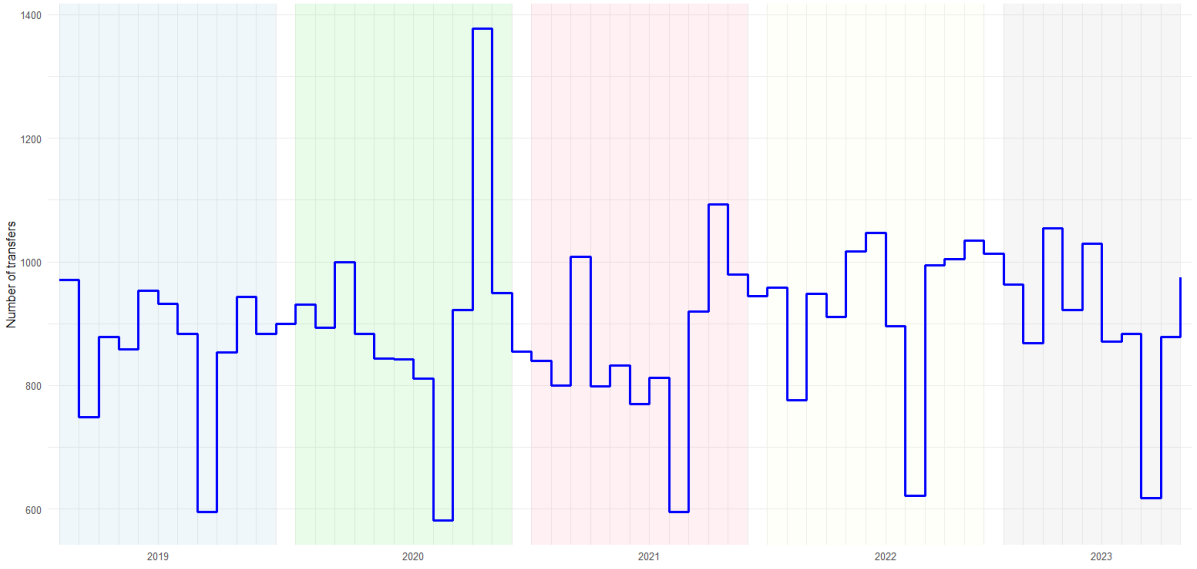

Figure 34. *Number of transfers in the intra-hospital network of GOMN over the study period.*

Looking at the modularity of the network, it can be seen in Figure 35 that decreased significantly in April 2020 (0.39) and was also low in October 2020 (0.49) in comparison with the other months (mean modularity over the study period =0.57).

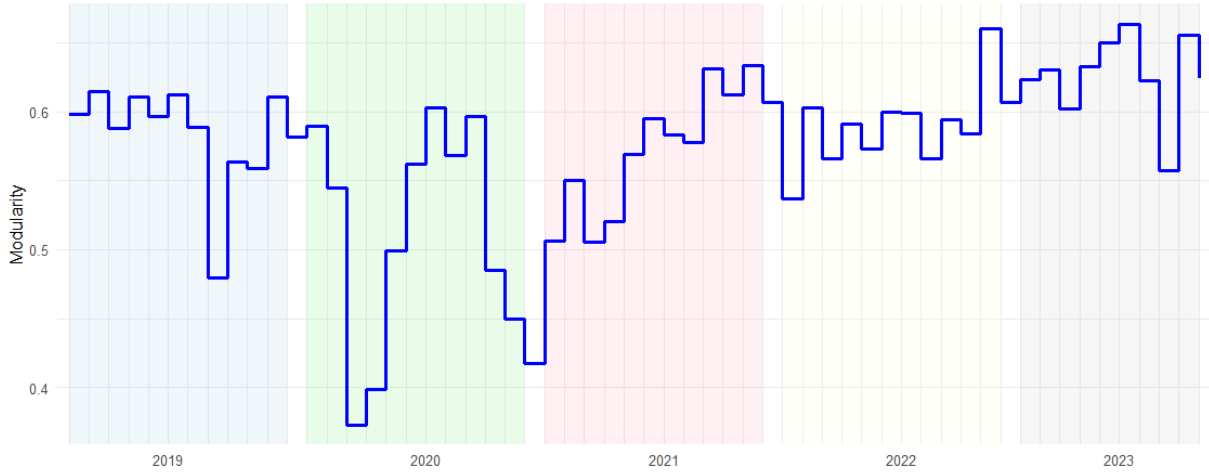

Figure 35. *Modularity of the intra-hospital network og GOMN over the study period.*

The number of links of the network, shown in Figure 36, similarly to the number of trasfers, show a slight decrease in April 2020 (318) and a peak in October 2020 (482) over the mean during the study period (mean number of links=360).

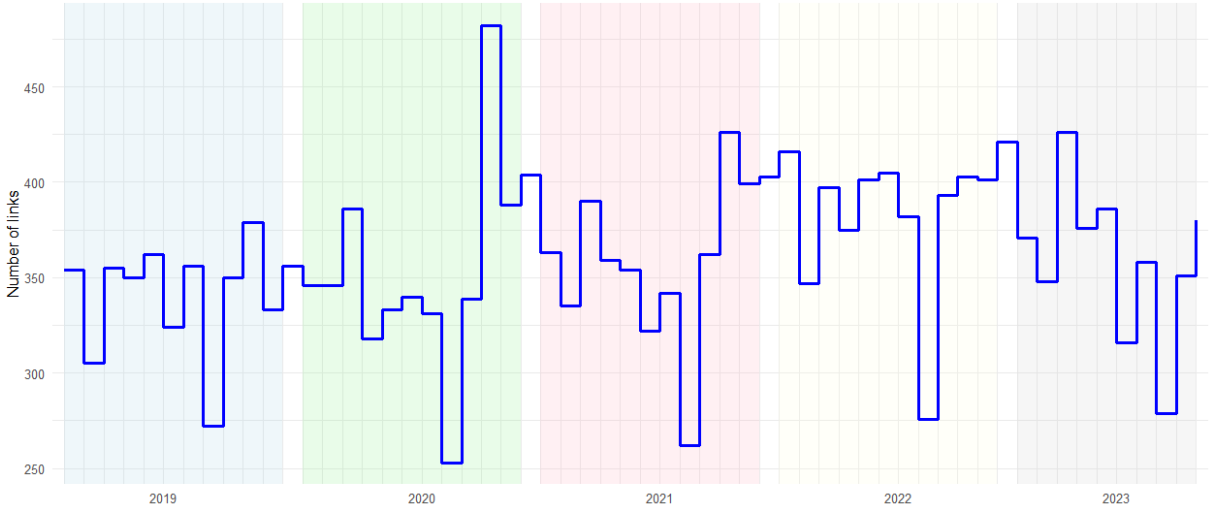

Figure 36. *Number of links in the intra-hospital network of GOMN over the study period.*

In Figure 37 it can be observed that in the months of August every year the network was more robust while the least robust month was October 2020 (t=187.0).

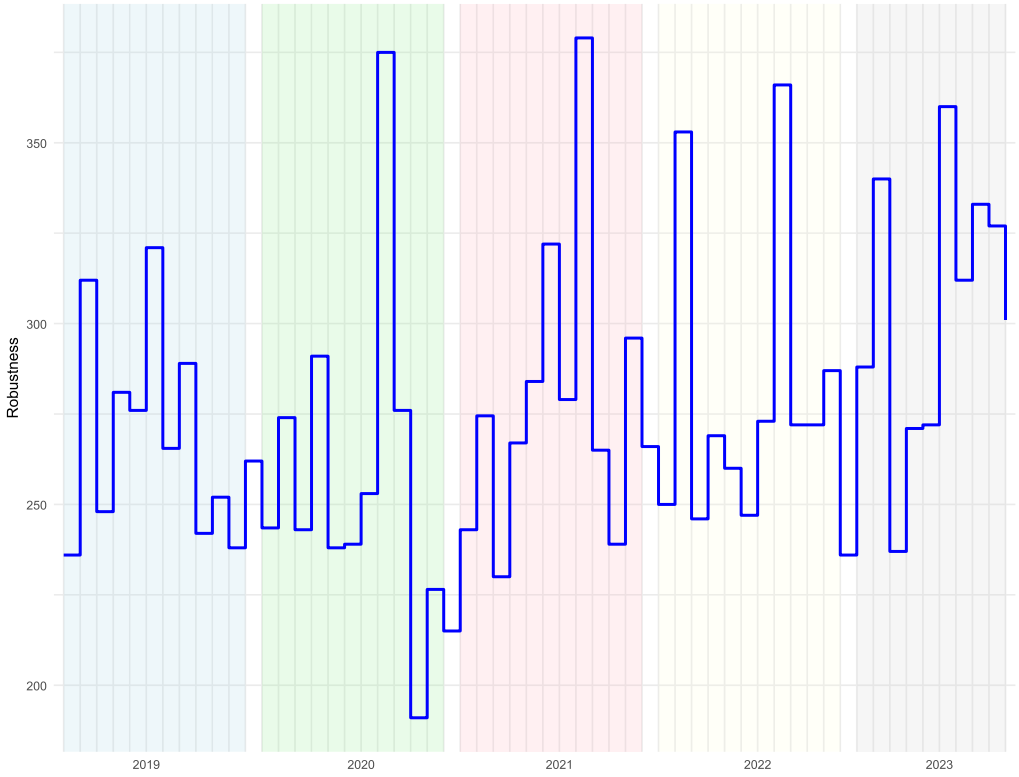

***Figure 37**. Robustness of the intra-hospital network over the study period for the GOMN wards.*

These results are also visible in the mean proportion of wards affected at each time step of the simulation for each year (Figure 38).

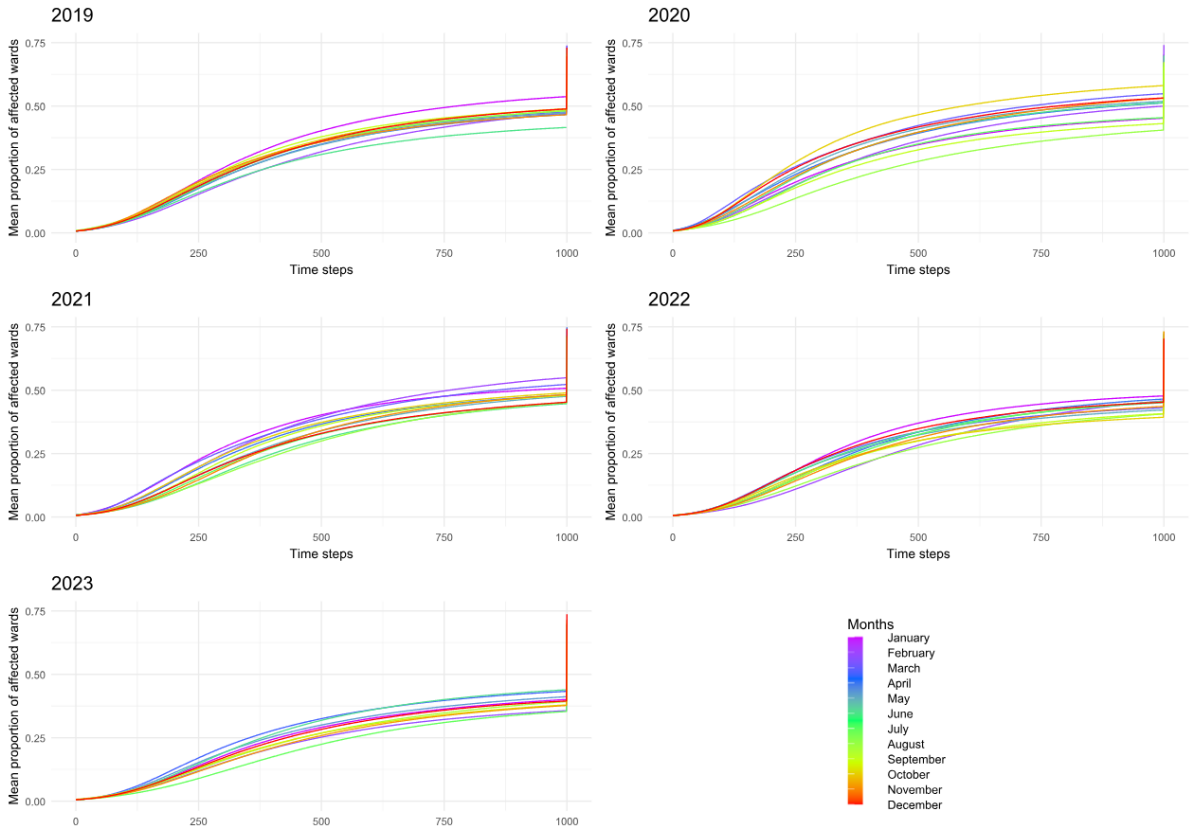

***Figure 38**. Mean proportion of wards affected at each time step of the simulation for each year for the dataset, coloured by month, based on the networks of the GOMN wards.*

An analysis of network robustness in relation to key structural parameters, namely, the number of links, modularity, and the number of patient transfers (Figure 39), shows a pattern in how these variables interact. The results suggest that network robustness tends to increase with higher levels of modularity, while it decreases as the number of transfers and links grows. These patterns are consistent across the observed data and suggest that both structural compartmentalization and mobility play significant roles in determining a hospital network's vulnerability to disruptions such as the spread of antimicrobial-resistant bacteria.

Figure 39. *Network robustness for GOMN according to A) transfers and modularity, B) number of links and modularity, C) transfers and number of links.*

5. Discussion

The findings of this study underlined that pandemic pressure, as well as internal and structural changes, influence the robustness of hospitals to the spread of antibiotic-resistant bacteria, effects that are detectable with network analysis. By examining the structure of wards, transfers and connections between wards, we can capture how the hospital dynamically reorganized under stress. Such changes directly influence the potential for pathogen spread, since they alter the number and type of contacts through which bacteria can circulate. More broadly, this emphasizes that infection risk is an emergent property of the connectivity of the system as a whole, not simply of local prevalence in isolated wards. Network analysis therefore offer a framework to interpret how external shocks, such as the SARS-CoV-2 pandemic, or other structural changes reshape the underlying architecture of healthcare and, in turn, the vulnerabilities of the hospital ecosystem.

5.1 UKF

This study indicates that the intra-hospital transfer network of the University hospital Freiburg (UKF) changed drastically during the COVID-19 pandemic, reflected in the higher robustness of the network against the spread of antibiotic-resistant bacteria (ABR) in April 2020. During this month, the time required for a potential ARB outbreak to disseminate throughout the intra-hospital network was longer than in any of the other months under investigation. In light of the organisational changes to the UKF brought about by the pandemic, it is plausible to suggest that the elevated robustness observed in April 2020 was a consequence of the restricted connections between the various departments, brought about by the suspension of elective surgeries and other deferrable procedures.

The intra-hospital network of the UKF remained relatively stable over the other months, quickly returning to previously observed robustness. However, from April 2021 onwards, we

observed a decline in robustness of the network, indicated by a more rapid dissemination of the bacteria in the simulation. A multitude of factors may have contributed to this observed change. Internal changes in structure, such as the opening of new wards and the formal merger with the Universitäts-Herzzentrum Freiburg – Bad Krozingen (UHZ) and the UKF in April 2021, may have contributed to this phenomenon, although not all of the newly established 39 wards were integrated into the network to the same extent.

The inclusion of more connected departments could facilitate the spread of ARB through the exchange of patients among the different wards, increasing the network's vulnerability to ARB outbreaks [68], [69]. Therefore, to compare the robustness of the network before and after the addition of new wards we decided to analyse the data excluding the new wards from our analysis. With this adjustment, we saw no big difference between the two periods before and after April 2021. Even though our network was relatively stable over time to external forces, the internal force of the addition of new wards affected its structure. For this reason, it is important to highlight that for network analysis the same networks should be compared, otherwise the measurements could be biased by the network size.

The strength of this study lies in the analysis of transfer data for five years from one of the largest hospitals in Germany. By using the network robustness as the primary metric, we were able to quantify the stability in risk of potential spread of ARB outbreaks in the hospital. This gives a clear indication of the influence of external forces on the network's robustness, and opens up possibilities for using health care policies to make hospitals more robust against ARB outbreaks. Therefore, an understanding of intra-hospital networks could have a significant impact on the strategies employed by hospitals to prevent the dissemination of ARB within and between wards [50].

5.2 GOMN

By reconstructing the real hospital network and simulating an outbreak of antibiotic-resistant bacteria (ARB) also within the GOMN hospital, we gained deeper insights into the key factors that influence network robustness. It is important to emphasize that the aim of this analysis was not to directly compare the simulation results across the two hospitals under study, as their structural and operational characteristics differ significantly. Any direct comparison would risk leading to misinterpretation and unwarranted conclusions.

In GOMN, the data from April 2020 reveal an interesting dynamic: although the number of admissions per day was lower compared to other months, the number of patient transfers remained relatively high (884). Specifically, the number of transfers in April 2020 was comparable to other months and even higher in October 2020 (1377). Additionally, the modularity of the network in both April and October 2020 was lower than in other months, indicating a more randomly connected network. (Q (modularity) = 0 means all connections are randomly distributed, =1 all connections are within clusters and not between clusters, <0 means it is more between than within).

Despite these structural similarities, network robustness displayed different behaviors. In April 2020, robustness remained comparable to other months, while in October 2020 it decreased significantly. This divergence suggests that multiple factors are at play in determining robustness. Based on our analysis, two main factors influence network robustness: the number of transfers and links among wards, and network modularity. A higher number of transfers and connections tends to reduce robustness, likely by facilitating wider pathogen spread. Conversely, greater modularity—indicating clearer compartmentalization of the network—tends to enhance robustness by containing potential outbreaks within sub-networks (clusters).

These findings underscore the importance of not only monitoring patient movement but also considering the structural organization of hospital networks when designing infection control strategies.

In fact, the observed difference in network robustness between April and October 2020, as illustrated in Figure 37, may be partially explained by the number of transfers, as shown in Figure 39. While modularity appears to play a role, its impact is only partial. The case of April 2020 stands out as an exception: we would have expected the network to exhibit lower robustness than it does. This discrepancy suggests that certain structural features of the network—beyond the number of transfers and probabilistic parameters used in the simulation—are influencing robustness in ways that are not fully captured by the current analysis.

5.3 Network analysis

This study's findings may aid public health policymakers strengthen infection control strategies by enhancing hospital network resilience. Our study suggests that intra-hospital patient transfer patterns can influence the spread of nosocomial pathogens, and external factors, such as the cancellation of elective surgeries during the pandemic, can enhance network robustness by reducing patient movement. Policy implications could include optimized patient transfer protocols with more structured patient transfer pathways to limit unnecessary movement within hospitals. Furthermore, hospitals could employ predictive analytics to anticipate how patient transfers affect the spread of pathogens: real-time monitoring of transfers may help detect risky patterns early. Implementing enhanced infection control measures, such as rigorous screening before transfers, dedicated transfer teams, and specialized cleaning protocols, may help contain potential outbreaks while maintaining essential hospital functions. If intra-hospital transfers influence pathogen spread,

inter-hospital patient movement may have similar effects; thus, a coordinated regional network approach, where hospitals collaborate to streamline transfers while reducing unnecessary movement, could further mitigate the risk of antimicrobial resistance spread.

Network analysis is an effective tool to describe systems behaviour and can help identify opportunities for intervention with targeted improvements, such as strategically locating and scaling resources, streamlining transfers, and ultimately providing patient-centered approaches to drive increased value. While previous studies have shown that the intra-hospital network is affected by the COVID-19 pandemic [70], the current study shows that this change is only temporarily, at least for the studied hospitals. Furthermore, the analysis also highlighted the impact of a change in internal structure and its importance when conducting this type of analysis.

The findings from GOMN highlight that network structure affects robustness independently of the number of transfers. In practical terms, this implies that while minimizing transfers may enhance robustness, it is not the only available strategy. Even when transfers are necessary, their configuration can be optimized to improve overall system resilience. Therefore, increasing robustness is not solely a matter of reducing movements, but also of strategically shaping transfer patterns to support structural stability. From a network perspective, this means that the position of transfers within the hospital graph—whether they occur between highly connected hubs, across modular boundaries, or through bridging wards—can determine the degree to which the system remains vulnerable to the spread of pathogens. For example, concentrating transfers within tightly clustered modules may limit cross-ward dissemination, while uncontrolled bridging across modules may facilitate rapid spread even if the total volume of transfers remains low. This distinction underscores the importance of considering not just the quantity of patient movement but also its quality in terms of network

topology. Ultimately, interventions aimed at strengthening hospital resilience should move beyond simplistic restrictions on transfers and instead incorporate strategies that deliberately reconfigure connectivity, prioritize safer pathways, and identify critical nodes whose protection or isolation can disproportionately enhance robustness.

5.4 Limitations

This study has some limitations that need to be considered when interpreting its results. First, the study uses only data on patient movements within the hospital, and no further data on the occurrence of ARB infections on the wards. The robustness against ARB spread is done based on simulated outbreaks. This is primarily done because the spread of ARB happens at a different timescale than the observed change in intra-hospital network structure. The influence of the network changes can therefore not be observed in the incidence of ARB from a single hospital, unless the network changes last longer.

Furthermore, it should be noted that the analysed data were only collected from single hospitals for each country. Although the principle behind the study should broadly apply, the question remains to what extent the specific results are applicable to other hospitals or healthcare facilities. Nonetheless, the findings of this study could assist public health policy makers in the design of new strategies to prevent the spread of ARB infections.

An additional limitation of this study is the lack of detailed information on whether patients had been transferred from long-term care facilities or external hospitals prior to admission; according to literature the prevalence of multidrug-resistant organisms is high both in long-term care acute facilities and nursing homes, exceeding the typical hospital prevalence of 10-15% [71], [72]. Although this information would be valuable given the recognised role of inter-facility movement in the spread of antimicrobial-resistant bacteria [73], [74], its impact in our setting is likely to be minimal. Previous internal analyses indicate that approximately 10% of

admitted patients had been hospitalised within the preceding two months; of these, only about 10% originated from an external hospital, while the remaining 90% were readmissions from another ward of the same institution. Thus, only around 1% of all admissions can be attributed to transfers from other hospitals. Moreover, the 30-day interval applied in our study captures the vast majority of readmissions to our own facility, as most readmissions occur within days or a few weeks of discharge [75], [76]. Given the relatively low prevalence of multidrug-resistant organisms in the general population [77] and the very limited proportion of patients transferred from external facilities, the potential influence of this limitation on our findings is considered negligible.

6. Conclusion

Analyzing intra-hospital patient transfer networks unveils hidden dynamics that are crucial for understanding how infections spread within hospitals, and consequently for improving infection control strategies.

This study advances our understanding of how antimicrobial resistance can spread through hospital networks, highlighting the importance of both structural and operational variables. By elucidating how network properties vary over time and in response to institutional or external events, our findings offer valuable insights for public health authorities. Specifically, the knowledge gained can support the development of targeted intervention strategies that take into account not just patient mobility, but also the underlying architecture of care delivery systems.

The overall structure of the Universitätsklinikum Freiburg (UKF) patient transfer network remained relatively stable throughout the study period, with the notable exception of April 2020. This deviation is likely attributable to the impact of the SARS-CoV-2 pandemic, particularly the hospital's response to the first wave. During this period, network robustness against simulated outbreaks of antibiotic-resistant bacteria (ARB) temporarily increased, suggesting that the hospital's pandemic response measures unintentionally contributed to greater structural resilience. However, this effect was short-lived, as the network rapidly returned to its typical configuration in the subsequent months.

In addition to the transient effects of the pandemic, longer-term structural changes within the hospital—such as a merger or reorganization—may have contributed to a gradual decline in robustness by altering the internal flow of patients. These institutional shifts could influence the connectivity of the network, thereby affecting its vulnerability to pathogen transmission.

Analysing network robustness in the context of a second hospital, GOMN, enabled a more nuanced understanding of the underlying mechanisms. Notably, we found that the structural configuration of the hospital network plays a critical role in determining robustness, independently of the sheer volume of patient transfers. In particular, factors such as the number of transfers and links, and the modularity of the network, were found to influence the capacity of the hospital to contain the spread of ARB.

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8. Appendix

***Table S 1**. Descriptive statistics of the complete data set of UKF.*

Year - Months	Unique patients	Wards	Connected wards	Mean indegree (wards)	Mean instrength (patients)	Mean length of stay (days)
2019						
January	10154	119	108	6.16	36.15	3.47
February	9700	118	105	5.80	34.95	3.57
March	10295	118	107	5.65	36.73	3.55
April	10025	120	110	5.53	35.71	3.42
May	10337	120	110	5.98	37.48	3.42
June	9564	118	105	5.93	37.00	3.48
July	10839	118	109	6.34	39.21	3.63
August	9777	121	107	6.01	37.46	3.62
September	9805	119	110	5.98	35.17	3.67
October	10174	123	110	6.24	35.78	3.69
November	9886	122	112	5.79	34.70	3.55
December	9186	119	108	5.80	34.76	3.39
2020						
January	10297	122	111	5.74	37.46	3.66
February	9651	119	107	5.96	34.92	3.68
March	8409	119	104	5.98	34.86	3.19
April	7139	110	102	4.40	30.50	3.34
May	8627	113	104	5.27	34.68	3.43
June	9501	116	106	5.83	35.60	3.27
July	10450	117	105	6.31	40.61	3.25
August	9682	113	105	6.03	38.09	3.57
September	9999	114	98	6.62	42.05	3.31
October	9839	117	104	5.85	38.00	3.73
November	9515	118	102	6.00	37.00	3.52
December	8484	115	105	5.68	33.95	3.29

2021						
January	8593	117	108	5.44	32.62	3.54
February	9018	119	106	5.88	34.70	3.48
March	10251	117	106	6.42	39.70	3.32
April	12144	137	128	6.16	39.79	3.49
May	11999	135	121	6.88	42.97	3.47
June	12443	140	127	6.71	41.63	3.26
July	13203	139	128	6.50	44.17	3.18
August	12676	137	122	7.06	45.45	3.57
September	12818	138	128	7.17	43.37	3.34
October	12890	137	122	7.07	44.67	3.54
November	12840	140	128	6.63	43.34	3.43
December	11234	138	122	6.61	40.93	3.45
2022						
January	11647	139	124	6.40	39.42	3.52
February	11805	141	125	6.44	39.14	3.45
March	13316	138	128	6.79	44.89	3.46
April	12300	141	128	6.77	42.74	3.25
May	13865	145	132	7.14	48.05	3.34
June	13038	143	132	7.27	46.53	3.40
July	13658	143	131	7.19	48.83	3.43
August	13477	145	133	7.00	46.71	3.29
September	13144	147	137	6.93	43.63	3.33
October	12361	141	130	7.07	45.05	3.29
November	12810	144	128	7.23	46.23	3.18
December	12455	145	131	7.11	44.72	3.25
2023						
January	12912	141	131	7.25	44.55	3.31
February	12794	143	130	7.12	44.96	3.29
March	14090	145	132	7.53	48.66	3.28
April	12354	146	131	7.18	43.85	3.37
May	13159	147	134	7.18	45.31	3.27
June	13192	144	129	6.95	48.11	3.33

July	13755	147	134	7.16	48.01	3.34
August	13409	145	135	7.52	45.76	3.22
September	12971	153	138	7.16	43.48	3.20
October	13503	147	135	7.40	46.55	3.25
November	13545	148	134	7.53	46.43	3.14
December	12342	147	128	7.52	45.51	3.09

***Table S 2**. Descriptive statistics including only the original UKF wards.*

Year - Months	Unique patients	Wards	Connected wards	Mean indegree (wards)	Mean instrength (patients)	Mean length of stay (days)
2019						
January	10154	119	108	6.16	36.15	3.47
February	9700	118	105	5.80	34.95	3.57
March	10295	118	107	5.65	36.73	3.55
April	10025	120	110	5.53	35.71	3.42
May	10337	120	110	5.98	37.48	3.42
June	9564	118	105	5.93	37.00	3.48
July	10839	118	109	6.34	39.21	3.63
August	9777	121	107	6.01	37.46	3.62
September	9805	119	110	5.98	35.17	3.67
October	10174	123	110	6.24	35.78	3.69
November	9886	122	112	5.79	34.70	3.55
December	9186	119	108	5.80	34.76	3.39
2020						
January	10297	122	111	5.74	37.46	3.66
February	9651	119	107	5.96	34.92	3.68
March	8409	119	104	5.98	34.86	3.19
April	7139	110	102	4.40	30.50	3.34
May	8627	113	104	5.27	34.68	3.43
June	9501	116	106	5.83	35.60	3.27
July	10450	117	105	6.31	40.61	3.25
August	9682	113	105	6.03	38.09	3.57
September	9999	114	98	6.62	42.05	3.31
October	9839	117	104	5.85	38.00	3.73
November	9515	118	102	6.00	37.00	3.52
December	8484	115	105	5.68	33.95	3.29
2021						
January	8593	117	108	5.44	32.62	3.54
February	9018	119	106	5.88	34.70	3.48

March	10250	116	105	6.46	40.06	3.35
April	9855	118	108	5.72	36.60	3.48
May	9788	116	102	6.45	39.70	3.54
June	10063	119	106	6.21	38.81	3.37
July	10654	118	106	6.04	40.83	3.19
August	10250	116	101	6.66	42.04	3.59
September	10382	117	107	6.57	40.15	3.34
October	10284	115	100	6.55	40.48	3.59
November	10200	118	105	6.12	38.93	3.49
December	9077	115	99	6.14	37.42	3.47
2022						
January	9286	117	98	6.12	36.97	3.58
February	9303	119	103	5.78	33.98	3.35
March	10444	116	105	6.35	39.44	3.50
April	9431	116	102	5.64	35.31	3.32
May	10568	117	104	6.11	40.22	3.40
June	9965	116	105	6.03	37.98	3.51
July	10477	116	104	5.88	40.08	3.55
August	10184	116	103	5.85	38.60	3.41
September	9945	119	108	5.75	35.04	3.43
October	9337	112	102	5.84	36.46	3.34
November	9749	116	100	6.00	38.25	3.26
December	9484	117	103	6.07	36.98	3.36
2023						
January	9753	113	104	5.99	36.27	3.39
February	9640	115	102	5.93	35.85	3.37
March	10473	116	104	6.16	38.11	3.37
April	9377	116	99	6.12	36.78	3.57
May	9860	117	105	5.94	36.40	3.38
June	9913	113	99	5.91	39.13	3.47
July	10376	116	103	6.10	39.62	3.37
August	10045	114	104	6.14	37.07	3.24
September	9849	121	105	6.08	36.68	3.33

October	10178	115	102	6.18	38.99	3.34
November	10214	114	102	6.53	37.93	3.30
December	9357	114	95	6.55	38.15	3.20

Table S 3. *Number of months in which each ward is included as a node in the network, as well as the specific months of inclusion. The original wards (last column) describes if a ward was included in the dataset containing only the original wards (+), or only in the complete dataset (-) for UKF.*

Abbreviations: Universitäts-Herzzentrum Freiburg – Bad Krozingen (UHZ); Universitätsklinik Freiburg (UKF).

Node	N. of months included	Months	Department	Original wards
1	60	All	Pain Centre, Tumour biology	+
2	60	All	Pain Centre, Tumour biology	+
3	60	All	Pain Centre, Tumour biology	+
4	60	All	Anaesthesiology and Critical Care	+
5	60	All	Anaesthesiology and Critical Care	+
6	60	All	Ophthalmology	+
7	60	All	Ophthalmology	+
8	60	All	Ophthalmology	+
9	60	All	Ophthalmology	+
10	60	All	Obstetrics and Gynaecology	+
11	60	All	General and Visceral Surgery	+
12	60	All	General and Visceral Surgery	+
13	60	All	Paediatric Surgery	+
14	60	All	General and Visceral Surgery	+
15	60	All	General and Visceral Surgery	+
16	60	All	General and Visceral Surgery	+
17	60	All	Orthopaedics and Trauma Surgery	+
18	60	All	Orthopaedics and Trauma Surgery	+

19	60	All	Thoracic Surgery	+
20	60	All	Thoracic Surgery	+
21	60	All	Urology	+
22	60	All	Urology	+
23	60	All	Urology	+
24	60	All	Plastic Surgery	+
25	60	All	Obstetrics and Gynaecology	+
26	60	All	Obstetrics and Gynaecology	+
27	60	All	Obstetrics and Gynaecology	+
28	60	All	Obstetrics and Gynaecology	+
29	60	All	Obstetrics and Gynaecology	+
30	60	All	Obstetrics and Gynaecology	+
31	60	All	Otolaryngology	+
32	60	All	Otolaryngology	+
33	60	All	Otolaryngology	+
34	60	All	Otolaryngology	+
35	60	All	Otolaryngology	+
36	60	All	Otolaryngology	+
37	60	All	Otolaryngology	+
38	60	All	Otolaryngology	+
39	60	All	Otolaryngology	+
40	60	All	Dermatology	+
41	60	All	Dermatology	+
42	60	All	Dermatology	+
43	60	All	Paediatrics	+
44	60	All	Paediatrics	+

45	60	All	Paediatrics	+
46	60	All	Paediatrics	+
47	60	All	Paediatrics	+
48	60	All	Paediatrics	+
49	60	All	Paediatrics	+
50	60	All	Paediatrics	+
51	60	All	Paediatrics	+
52	60	All	Paediatrics	+
53	60	All	Paediatrics	+
54	60	All	Tumour Centre, Tumour biology	+
55	60	All	Tumour Centre, Tumour biology	+
56	60	All	Tumour Centre, Tumour biology	+
57	60	All	Tumour Centre, Tumour biology	+
58	60	All	Tumour biology	+
59	60	All	Internal Medicine	+
60	60	All	Internal Medicine	+
61	60	All	Internal Medicine	+
62	60	All	Internal Medicine	+
63	60	All	Internal Medicine	+
64	60	All	Internal Medicine	+
65	60	All	Internal Medicine	+
66	60	All	Internal Medicine	+
67	60	All	Internal Medicine	+
68	60	All	Otolaryngology	+

69	60	All	Emergency Medicine	+
70	60	All	Neurosurgery	+
71	60	All	Neurosurgery	+
72	60	All	Neurosurgery	+
73	60	All	Neurosurgery	+
74	60	All	Neurosurgery	+
75	60	All	Neurosurgery	+
76	60	All	Neurosurgery	+
77	60	All	Neurology	+
78	60	All	Neurology	+
79	60	All	Neurology	+
80	60	All	Neurology	+
81	60	All	Psychiatry and Psychotherapy	+
82	60	All	Psychiatry and Psychotherapy	+
83	60	All	Psychiatry and Psychotherapy	+
84	60	All	Psychiatry and Psychotherapy	+
85	60	All	Psychiatry and Psychotherapy	+
86	60	All	Psychiatry and Psychotherapy	+
87	60	All	Psychiatry and Psychotherapy	+
88	60	All	Psychiatry and Psychotherapy	+
89	60	All	Psychiatry and Psychotherapy	+

90	60	All	Psychosomatic Medicine and Psychotherapy	+
91	60	All	Psychosomatic Medicine and Psychotherapy	+
92	60	All	Child and Adolescent Psychiatry	+
93	60	All	Child and Adolescent Psychiatry	+
94	60	All	Child and Adolescent Psychiatry	+
95	60	All	Radiation Oncology	+
96	60	All	Nuclear Medicine	+
97	60	All	Dental Medicine	+
98	60	All	Palliative Medicine	+
99	59	All except April 2020	Ophthalmology	+
100	59	All except April 2020	Orthopaedics and Trauma Surgery	+
101	59	All except April 2020	Otolaryngology	+
102	59	All except April 2020	Rheumatology	+
103	59	All except October 2022	Neurosurgery	+
104	59	All except October 2022	Neurosurgery	+
105	54	All except April-September 2020	Tumour biology	+
106	54	All except April-September 2020	Thoracic Surgery	+
107	54	All except April-September 2020	Tumour biology	+
108	54	All except June-August 2023 and October-December 2023	Radiology	+
109	50	All except January-October 2019	Neurology	+

110	47	All except July 2019, September 2019, December 2019, December 2020, January 2021, March-April 2021, October-December 2021, October-December 2023	Neurosurgery	+
111	47	October 2019-April 2020, July 2020, October 2020-December 2023	Tumour biology	+
112	45	April 2020-December 2023	Neurosurgery	+
113	39	All except March 2019, September 2019, March-April 2020, October 2020, December 2020, February 2021, June 2021, January-April 2022, June 2022, September 2022, December 2022-February 2023, June-August 2023, December 2023	Neurosurgery	+
114	38	February 2019-July 2019, September 2019-June 2020, September 2020-April 2021, June 2021, November 2021-February 2022, May 2022, September 2022, December 2022, February 2023, May-July 2023, September 2023, December 2023	Tumour biology	+
115	35	All except April-May 2020, November-December 2020, April-May 2021, October 2021, February 2022, April-July 2022, October-November 2022, January 2023-October 2023, December 2023	Urology	+
116	35	July 2020-February 2021, April-November 2021, February-September 2022, December 2022, March-December 2023	Neurosurgery/Pain Centre, Tumour biology	+

117	33	April 2021-December 2023	Bariatric and Metabolic Surgery (UHZ)	-
118	33	April 2021-December 2023	Transfer from UHZ to UKF	-
119	33	April 2021-December 2023	Cardiology (UHZ)	-
120	33	April 2021-December 2023	Cardiology (UHZ)	-
121	33	April 2021-December 2023	Cardiology	-
122	33	April 2021-December 2023	Cardiology	-
123	33	April 2021-December 2023	Cardiology	-
124	33	April 2021-December 2023	Cardiology	-
125	33	April 2021-December 2023	Cardiology (UHZ)	-
126	33	April 2021-December 2023	Cardiology (UHZ)	-
127	33	April 2021-December 2023	Cardiology (UHZ)	-
128	33	April 2021-December 2023	Cardiology (UHZ)	-
129	33	April 2021-December 2023	Cardiology (UHZ)	-
130	33	April 2021-December 2023	Cardiology (UHZ)	-
131	33	April 2021-December 2023	Cardiology (UHZ)	-
132	33	April 2021-December 2023	Cardiology	-
133	33	April 2021-December 2023	Cardiology	-
134	33	April 2021-December 2023	Cardiology (UHZ)	-
135	31	April 2021-May 2022, August 2022-December 2023	Cardiology (UHZ)	-
136	31	June 2021-December 2023	Plastic Surgery	-
137	30	July 2021-December 2023	Geriatric Medicine and Gerontology	-
138	28	January 2019-December 2020, March-June 2021	Plastic Surgery	+
139	27	October 2021-December 2023	Orthopaedics and Trauma Surgery	-

140	22	January 2020, April 2021, September 2022, November-December 2022, February 2023, May 2023, July-September 2023	Obstetrics and Gynaecology	+
141	21	June 2020, November 2021, February-November 2022, January-May 2023, July 2023, October-December 2023	Urology	+
142	21	April 2022-December 2023	Anaesthesiology and Intensive Care	-
143	21	April 2022-December 2023	Anaesthesiology and Intensive Care	-
144	21	April 2022-December 2023	Anaesthesiology and Intensive Care	-
145	20	May 2022-December 2023	Anaesthesiology and Intensive Care	-
146	20	May 2022-December 2023	Cardiology (UHZ)	-
147	20	May 2022-December 2023	Child and Adolescent Psychiatry	-
148	19	April-November 2020, September 2021, November 2021, January 2022, March-April 2022, July 2022, November-December 2022, July 2023, September-October 2023	Cardiovascular Surgery	+
149	16	January 2019-April 2020	Neurology	+
150	15	January 2019-March 2020	Tumour biology	+
151	15	January 2019-March 2020	Urology	+
152	15	January 2019-March 2020	Neurology	+
153	13	March-May 2019, October 2019, January 2020, May-July 2020, February 2021, September-October 2021, January-February 2022	Oral and maxillofacial surgery	+

154	10	August-October 2019, June 2021, October 2021-February 2022, December 2023	Obstetrics and Gynaecology	+
155	10	March 2023-December 2023	Cardiology (UHZ)	-
156	9	January 2019, September-November 2019, February 2021, July 2021, September 2022, April 2023	Paediatric Surgery	+
157	9	November 2019, March 2020, June-July 2020, January 2021, April 2021, May-June 2022, September 2023	General and Visceral Surgery	+
158	9	November 2020-July 2021	Anaesthesiology and Intensive Care	+
159	8	May-December 2023	Tumour biology	-
160	7	April-May 2019, August-September 2019, February 2021, March 2023	Neurology	+
161	6	July-December 2023	Oral and maxillofacial surgery	-
162	5	July-August 2019, April 2021, July-August 2021	Neurosurgery	+
163	5	August 2019, February 2022, August-October 2023	Orthopaedics and Trauma Surgery	+
164	5	January 2020, June 2021, June 2022, September 2022, September 2023	Orthopaedics and Trauma Surgery	+
165	4	September-December 2023	Cardiovascular Surgery	-
166	2	April 2020, September 2023	Orthopaedics and Trauma Surgery	+
167	2	March 2021, August 2022	Outpatient Clinic	-
168	2	October 2022, June 2023	Ophthalmology	-
169	2	November, December 2023	Neurosurgery	-
170	1	January 2019	Tumour biology	+

171	1	July 2020	Obstetrics and Gynaecology	+
172	1	June 2021	Obstetrics and Gynaecology	-
173	1	December 2021	Thoracic Surgery	-
174	1	April 2023	Internal Medicine	-
175	1	November 2023	Plastic Surgery	-

Table S 4. *Descriptive statistics of the data set for GOMN.*

Year - Months	Unique patients	Wards	Connected wards	Mean indegree (wards)	Mean instrength (patients)	Mean length of stay (days)
2019						
January	4634	141	106	3.34	9.16	5.99
February	4282	134	99	3.08	7.57	6.12
March	4690	141	104	3.41	8.45	5.69
April	4430	140	106	3.30	8.10	7.07
May	4917	142	110	3.29	8.66	5.79
June	4611	140	111	2.92	8.40	5.62
July	4460	140	109	3.27	8.11	5.98
August	2784	106	75	3.63	7.93	8.06
September	4612	135	98	3.57	8.70	6.34
October	5030	141	112	3.38	8.42	5.97
November	4602	138	96	3.47	9.21	5.58
December	4298	141	103	3.46	8.74	6.73
2020						
January	4623	138	97	3.57	9.60	6.26
February	4190	135	100	3.46	8.93	5.40
March	3405	110	90	4.29	11.11	7.01
April	2986	100	86	3.70	10.28	8.47
May	3287	115	87	3.83	9.70	6.94
June	3815	130	91	3.74	9.25	6.30
July	3856	136	91	3.64	8.91	5.93
August	2841	119	78	3.24	7.45	6.50
September	4290	144	97	3.49	9.51	6.11
October	5019	149	114	4.23	12.08	5.76
November	3805	128	101	3.84	9.41	6.21
December	3407	123	93	4.34	9.19	6.89
2021						
January	3476	119	92	3.95	9.13	7.09
February	3681	122	99	3.38	8.08	7.41

March	4342	136	105	3.71	9.60	6.86
April	3894	135	101	3.55	7.90	7.46
May	4042	147	103	3.44	8.08	6.45
June	4240	144	103	3.13	7.48	6.51
July	4157	150	107	3.20	7.59	6.09
August	2822	116	82	3.20	7.26	8.12
September	4761	152	115	3.15	7.99	6.16
October	5016	159	120	3.55	9.11	5.96
November	5042	161	122	3.27	8.03	5.94
December	4377	159	118	3.42	8.00	5.82
2022						
January	3971	157	113	3.68	8.48	6.94
February	3991	156	119	2.92	6.52	6.41
March	4754	161	113	3.51	8.39	7.41
April	4476	165	117	3.21	7.79	6.07
May	5145	169	121	3.31	8.40	5.75
June	4871	173	121	3.35	8.65	5.92
July	4443	170	123	3.11	7.28	5.38
August	2962	136	96	2.88	6.48	7.13
September	4821	171	125	3.14	7.96	6.29
October	4959	174	120	3.36	8.37	6.15
November	5067	179	131	3.06	7.89	5.39
December	4387	172	121	3.48	8.37	5.90
2023						
January	4554	175	122	3.04	7.89	6.69
February	4511	179	121	2.88	7.17	5.39
March	5002	184	119	3.58	8.86	5.22
April	4252	175	116	3.24	7.95	5.82
May	4943	176	122	3.16	8.43	5.73
June	4570	181	114	2.77	7.64	5.69
July	4484	181	127	2.82	6.96	5.45
August	2918	139	91	3.07	6.79	6.20
September	4680	175	125	2.81	7.03	5.96

October	4991	179	132	2.88	7.39	5.48

Table S 5. *Number of months in which each ward is included as a node in the network, as well as the specific months of inclusion for GOMN.*

Node	N. of months included	Months	Department
1	58	All	Oncology Day Hospital
2	58	All	Haematology Day Hospital
3	58	All	Bone Marrow Transplant Centre Day Hospital
4	58	All	Oncology Day Hospital
5	58	All	Cardiology Day Hospital
6	58	All	Allergology and Immunology Day Hospital
7	58	All	Cardiology
8	58	All	Cardiology
9	58	All	Cardiology
10	58	All	Paediatric Cardiology
11	58	All	Cardiology
12	58	All	Cardiology
13	58	All	General, Oncologic and Minimally Invasive Surgery
14	58	All	General, Oncologic and Minimally Invasive Surgery
15	58	All	General and Transplant Surgery
16	58	All	General and Transplant Surgery
17	58	All	Orthopaedics and Trauma Surgery
18	58	All	Oral and Maxillofacial Surgery

19	58	All	Paediatric Surgery
20	58	All	Plastic Surgery
21	58	All	Thoracic Surgery
22	58	All	Vascular Surgery
23	58	All	Haematology
24	58	All	Haematology
25	58	All	Haematology
26	58	All	Bone Marrow Transplant Centre
27	58	All	Infectious Diseases
28	58	All	Internal Medicine
29	58	All	Internal Medicine
30	58	All	Emergency Medicine
31	58	All	Neurosurgery
32	58	All	Neurosurgery
33	58	All	Neonatology and Neonatal Intensive Care Unit
34	58	All	Neurology and Stroke Unit
35	58	All	Stroke Unit
36	58	All	Orthopaedics and Trauma Surgery
37	58	All	Obstetrics and Gynaecology
38	58	All	Obstetrics and Gynaecology
39	58	All	Otolaryngology
40	58	All	Paediatrics
41	58	All	Psychiatry
42	58	All	Psychiatry

43	58	All	Urology
44	58	All	Urology
45	58	All	Plastic Surgery
46	58	All	Nephrology
47	58	All	Nephrology Day Hospital
48	58	All	Nephrology
49	58	All	Anaesthesiology and Intensive Care
50	58	All	Anaesthesiology and Intensive Care
51	58	All	Neurocritical Care
52	58	All	Anaesthesiology and Intensive Care
53	58	All	Coronary Care Unit
54	58	All	Rehabilitation Medicine and Neurorehabilitation
55	58	All	Hepatology and Gastroenterology
56	58	All	Hepatology and Gastroenterology Day Hospital
57	58	All	Liver Unit
58	58	All	Oncology
59	58	All	Rheumatology Day Hospital
60	58	All	Neonatology and Neonatal Intensive Care Unit
61	58	All	Pain Therapy Day Surgery
62	58	All	Obstetrics and Gynaecology Day Surgery
63	58	All	Neuroradiology Day Surgery

64	58	All	Paediatric Ophthalmology Day Surgery
65	58	All	Paediatrics Day Hospital
66	58	All	Palliative Care and Hospice
67	57	All except August 2022	Endocrinology Day Hospital
68	57	All except April 2020	Cardiovascular Surgery
69	57	All except January 2023	Cardiology
70	57	All except October 2023	Internal Medicine
71	57	All except August 2023	Internal Medicine
72	57	All except October 2023	Internal Medicine
73	57	All except April 2020	Centre for the Study and Treatment of Fertility Disorders Day Hospital
74	57	All except August 2019	Pain Therapy Week Hospital
75	57	All except May 2020	Child and Adolescent Neuropsychiatry Day Hospital
76	56	All except August 2019, August 2022	Cardiology Week Hospital
77	56	All except March-April 2020	Radiology Week Hospital
78	56	All except May-June 2021	Clinical Dietetics and Nutrition Day Hospital
79	56	All except August 2019, August 2023	Nuclear Medicine
80	56	All except March-April 2020	Ophthalmology Day Hospital
81	55	All except August 2021, August 2022, August 2023	Ophthalmology
82	55	All except March 2020, December 2020, January 2022	Orthopaedics and Trauma Surgery
83	55	All except March-April 2020, August 2020	Urology Day Surgery
84	54	All except April 2020, March-April 2021, July 2021	Paediatrics

85	54	All except August 2019, April 2020, August 2020, August 2021	Paediatric Surgery Day Surgery
86	53	All except August 2019, March-April 2020, June-July 2020	Cardiology Week Hospital
87	53	All except November 2020-March 2021	Clinical Dietetics and Nutrition
88	53	All except August 2019, October 2021, July 2022, November 2022, August 2023	Neurology and Stroke Unit Day Hospital
89	53	All except March-April 2020, February 2021, April 2021, August 2021	General Surgery Day Surgery
90	53	All except August 2019, March-April 2020, November 2020, August 2023	Radiology Day Surgery
91	53	All except April 2020, January-March 2021, January 2022	Otorhinolaryngology Day Surgery
92	53	All except August 2019, April-May 2020, August 2020, August 2022	Paediatric Cardiology Day Surgery
93	52	All except April-September 2021	Haematology Day Surgery
94	52	All except August 2019, April-May 2020, February 2022, August 2022, August 2023	Epilepsy and Parkinson's Surgery
95	51	All except August 2019, March-April 2020, January 2021, August 2021, August 2022, August 2023	Cardiology Day Surgery
96	51	All except April 2020, November 2020-April 2021	Pneumology
97	51	All except March-April 2020, August 2020, February 2021, July 2021, August 2022, August 2023	Plastic Surgery Day Surgery
98	50	All except August 2019, March-August 2020, August 2021	Cardiology Week Hospital
99	50	All except November 2019, March-May 2020, September 2020, November 2020-January 2021	Paediatrics Cardiology
100	50	All except February 2019, April-May 2020, August 2020, December 2020, June 2021, March 2023	Oncology
101	49	All except April-May 2020, November 2020-April 2021, August 2023	Allergology and Immunology
102	49	All except February 2019, April 2019, April 2020, February 2021, August 2022, October 2022, February 2023, April 2023, August 2023	Diabetology Day Hospital

103	49	All except August 2019, May-August 2020, April-June 2021, August 2021	Cardiology Week Hospital
104	49	All except April-May 2020, November 2020-April 2021, August 2023	Endocrinology
105	49	All except August-September 2019, April 2020, January 2021, September 2021, January 2022, April 2022, January-February 2023	Obstetrics and Gynaecology
106	49	All except April-May 2020, November 2020-April 2021, August 2023	Rheumatology
107	49	All except March-April 2020, August 2020, November 2020-February 2021, August 2021, August 2023	Digestive and Interventional Endoscopy Day Surgery
108	49	All except January-August 2019, March 2020	Digestive and Interventional Endoscopy Week Hospital
109	48	All except August 2019, March-May 2020, November 2020-Februar 2021, August 2021, January 2022	General and Transplant Surgery Week Hospital
110	48	All except March-May 2020, November 2020-February 2021, August 2021, February 2022, August 2022	Urology
111	48	All except August 2019, March-June 2020, August 2020, November 2020-January 2021, August 2021	Thoracic Surgery Day Surgery
112	47	All except August-September 2019, February-May 2020, November 2020-January 2021, August 2021, August 2022	Oncologic and Minimally Invasive General Surgery
113	47	All except December 2020-February 2021, May-September 2021, December 2021-February 2022	General Sub-Intensive Care
114	47	All except August 2019, March-May 2020, January-June 2021, August 2021	Day Surgery, Week Surgery
115	47	All except January 2019, April 2019, September 2019, March 2020, December 2021, December 2022, April-August 2023	Paediatric Ophthalmology
116	46	All except April-May 2020, October 2020-February 2021, April-August 2021	Infectious Diseases Day Hospital
117	45	All except February 2019, August 2019, November 2019, January 2020, June-July 2020, June-July 2021, July-September 2022, October 2023	Vascular Surgery
118	45	All except March-June 2020, January-April 2021, May 2021, August 2021, February 2022, December 2022, August 2023	Orthopaedics and Traumatology Day Surgery

119	44	All except April–August 2020, January–June 2021, August–September 2021, August 2023	Paediatric Surgery
120	44	All except March 2019, June 2019, August 2019, April–August 2020, October–November 2021, July 2022, February 2023, June 2023, October 2023	Geriatric Rehabilitation Medicine and Neurorehabilitation
121	43	All except June–August 2019, December 2019–January 2020, March–May 2020, November–December 2020, January–February 2021, August 2021, August 2022, August 2023	Obstetrics and Gynaecology
122	43	All except January–August 2019, March–April 2020, December 2020, February 2021, April–May 2021, January 2022	Oncologic and Minimally Invasive General Surgery Week Hospital
123	43	All except January–August 2019, March–May 2020, November–December 2020, August 2022, August 2023	Urology Neuro-Urology
124	42	All except April–May 2019, November 2019, January 2020, August 2020, November–December 2020, February 2021, May–August 2021, February–March 2022, September 2022, August 2023	Cardiovascular Surgery
125	42	All except August 2019, March–August 2020, November 2020-June 2021, August 2021	Vascular Surgery Week Hospital
126	39	All except August 2019, March–August 2020, November 2020–April 2021, June 2021, August 2021, August–September 2022, November 2022, August 2023	Paediatric Cardiology Week Hospital
127	39	All except August 2019, March–August 2020, November 2020–July 2021, January 2022, March 2022, July–September 2022	Urology Week Hospital
128	38	All except August 2019, March–August 2020, December 2020–September 2021, January 2022, June 2023, August 2023	Paediatric Ophthalmology Week Hospital
129	38	All except August 2019, March–June 2020, November 2020, January–September 2021, December 2021–February 2022, August 2022, August 2023	Obstetrics and Gynaecology Week Hospital
130	37	All except January–August 2019, March–May 2020, November 2020–May 2021, August 2021, January–February 2022	Day Surgery, Week Surgery, Week Hospital
131	35	All except February–October 2019, February–May 2020, July–August 2020, October–December 2020, January–February 2021, August 2021, October	Digestive and Interventional Endoscopy

		2021, February–March 2022, August 2022, November 2022, June 2023, August 2023	
132	35	All except January–December 2019, January–May 2020, November–December 2020, January 2021, August 2021, February 2022, April 2022, August 2022, August 2023	Neurosurgery
133	34	January 2019–May 2021, December 2021, April 2022, August 2022, October 2022, December 2022	Neonatology and Neonatal Intensive Care
134	34	January 2021–October 2023	Neonatology and Neonatal Intensive Care
135	34	January 2021–October 2023	Neonatology and Neonatal Intensive Care
136	32	All except August 2019, February 2020, April–July 2020, October 2020, November–December 2020, June–September 2021, January–February 2022, December 2022, January 2023	Thoracic Surgery Week Hospital
137	32	All except July–October 2019, February–September 2020, November 2020, January 2021, March 2021, June 2021, August 2021, December 2021, March–June 2022, September 2022, November 2022, January–February 2023, July 2023	Radiology
138	32	All except January 2019–August 2020, November 2020–February 2021, June 2022, October 2022	Wound Care and Diabetic Foot
139	31	April 2021–October 2021, December 2021–October 2023	Neurology
140	31	April 2021–October 2023	Epilepsy and Parkinson's Surgery
141	30	January 2019, March–May 2019, July 2019, September 2019, December 2019, June 2020, October 2021, November 2021–February 2022, April–May 2023, September–October 2023	Cardiology
142	30	January–February 2019, May–July 2019, October–December 2019, January–February 2020, June–July 2020, October 2020, November 2020, January–February 2021, June–July 2021, October 2021, November 2021, January–February 2022, May–June 2022, October 2022, January–February 2023, May 2023, August 2023, October 2023	General and Transplant Surgery

143	30	January 2019–August 2020, October 2020, December 2020–January 2021, March–April 2021, July 2021	Otorhinolaryngology
144	29	July 2020, September-October 2020, February 2021, June-July 2021, September-December 2021, March-July 2022, September 2022-October 2023	Burns and Reconstructive Plastic Surgery Centre
145	29	September-October 2020, February 2021, April 2021, June 2021-July 2022, October 2022-January 2023, March-June 2023, August-October 2023	Emergency and Major Trauma Surgery
146	28	November 2020-May 2021, November 2021-May 2023, September-October 2023	COVID Internal Medicine
147	28	July 2021-October 2023	Pneumology
148	27	March-July 2021, September-December 2021, March-July 2022, September-December 2022, February-October 2023	Pain Therapy
149	27	May-July 2021, September 2021-June 2022, August 2022-July 2023, September-October 2023	Otorhinolaryngology
150	26	July 2020, July 2021, September 2021-July 2022, September 2022-July 2023, September-October 2023	Ophthalmology
151	26	May-July 2021, September 2021-July 2022, September 2022-March 2023, June-October 2023	Neurosurgery
152	25	January 2019, March 2019, July 2019, November 2019, January 2020, March 2020, May 2020, July 2020, September-October 2020, October-November 2021, April-June 2022, September 2022-April 2023, June 2023, October 2023	Paediatric Cardiology
153	25	May–July 2021, September 2021–January 2022, March–July 2022, September–November 2022, January–May 2023, July–October 2023	Orthopaedics and Traumatology
154	24	January 2019 – October 2020, July–August 2021	Thoracis Surgery
155	24	March 2019, December 2019, April–July 2021, November 2021, March–June 2022, September–December 2022, January–June 2023, August–October 2023	Vascular Surgery
156	24	June–July 2019, December 2019, April–May 2020, March 2021, October–November 2021, April–December 2022, January–May 2023, August 2023, October 2023	Haematology

157	23	January 2019, April 2019, June 2019, September 2019, November 2019, January–May 2020, September–December 2020, January 2021, May–July 2021, October 2021, February 2022, July 2022, August 2023, October 2023	Thoracis Surgery
158	23	June 2019, September 2020, November 2020, January 2021, April–May 2021, July 2021, November–December 2021, February 2022, April–July 2022, September–October 2022, February 2023, May–August 2023, September–October 2023	Cardiology
159	23	May–July 2021, September–December 2021, March–July 2022, October–November 2022, January–July 2023, September–October 2023	Orthopaedics and Traumatology
160	22	April 2019, August 2019, January 2020, July 2020, May–June 2021, November 2021, March–April 2022, June–July 2022, October–December 2022, January–July 2023, October 2023	Cardiology
161	22	October 2020–April 2022, June 2022, February 2023, May 2023	COVID Intensive Care
162	21	January 2019, March–April 2019, June 2019, November 2019, April–May 2020, August–September 2020, November 2020–February 2021, December 2021, February 2022, May 2022, November 2022-January 2023, June–July 2023	Cardiology
163	21	January 2019, June–July 2020, September 2020, March–July 2021, September–December 2021, April–June 2022, December 2022, March–April 2023, July 2023, October 2023	Otorhinolaryngology
164	21	May–July 2021, September 2021–May 2022, January–July 2023, September–October 2023	Diabetology
165	18	May 2022–October 2023	Obstetrics and Gynaecology
166	17	October–December 2020, October 2021, December 2021, July 2022, October 2022–August 2023	COVID Internal Medicine
167	17	June 2022–October 2023	Maxillofacial Surgery Week Hospital
168	17	June 2022–October 2023	Neurosurgery Day Surgery

169	16	March–May 2019, October 2019, December 2019, April–May 2020, November 2020–January 2021, April 2021, June 2021, October–November 2021, February 2022, February 2023	Cardiology
170	16	October 2021, December 2021–May 2022, September 2022, December 2022, March–August 2023	Burns and Reconstructive Plastic Surgery Centre
171	16	January–May 2022, July 2022, December 2022, January–September 2023	Neurosurgery
172	16	June–July 2022, September 2022–October 2023	Burns and Reconstructive Plastic Surgery Centre Day Surgery
173	15	April–May 2019, July–August 2019, October 2019, December 2019–January 2020, October 2020, April 2021, July 2022, October 2022, January 2023, July–September 2023	Thoracic Surgery
174	15	June–July 2022, September 2022–July 2023, September–October 2023	Tissue Bank and Tissue Therapy Week Hospital 2
175	15	July 2022–July 2023, September–October 2023	Emergency and Major Trauma Surgery
176	14	March–June 2020, November 2020, February–May 2021, September 2021, June–July 2022, September 2022, July 2023	COVID Anaesthesia and Intensive Care
177	14	July 2020, September 2020, May–June 2021, November 2021, May–July 2022, October 2022, January 2023, April–July 2023	Emergency and Major Trauma Surgery
178	14	October–December 2020, March–May 2021, September 2021, December 2021–February 2022, November 2022–January 2023, June 2023	COVID Emergency Medicine
179	14	June–July 2022, September 2022–April 2023, June–July 2023, September–October 2023	Burns and Reconstructive Plastic Surgery Centre Week Hospital
180	14	June–July 2022, September 2022–July 2023, October 2023	Orthopaedics and Traumatology Week Hospital
181	13	January–May 2022, July–August 2022, November–December 2022, February–March 2023, September–October 2023	COVID Orthopaedics and Traumatology

182	13	February 2022–February 2023	COVID Infectious Diseases Day Hospital
183	13	July–October 2022, December 2022–March 2023, May–August 2023, October 2023	Geriatric Rehabilitation Medicine and Neurorehabilitation
184	12	April–June 2020, October–December 2020, March 2021, January–May 2022	COVID Surgery
185	12	June–July 2021, September 2021, December 2021–June 2022, November 2022, March 2023	Emergency and Major Trauma Surgery
186	12	June–September 2021, September–October 2022, January–February 2023, June–July 2023, September–October 2023	Oncology
187	12	January–May 2022, July–August 2022, October–December 2022, June 2023, October 2023	COVID Neurology
188	11	May 2019, October 2019, July 2020, April–June 2021, December 2021, March 2022, September 2022, February–March 2023	Cardiovascular Surgery
189	11	January–February 2022, July–August 2022, November 2022–January 2023, April 2023, June–July 2023, October 2023	COVID Cardiology
190	11	April–December 2022, June–July 2023	Tissue Bank and Tissue Therapy Day Surgery
191	10	January–July 2019, October 2019, October 2020, October 2022	Oncologic and Minimally Invasive General Surgery Week Hospital
192	10	March 2019, May-July 2019, October 2019, May 2020, November-December 2021, September 2022, September 2023	General and Transplant Surgery Day Surgery
193	10	March-June 2020, November 2020-February 2021, December 2021-Janaury 2022	Subacute Care
194	10	October 2020-February 2021, April 2021, September 2021, January 2022, March 2022, October 2023	COVID
195	9	March-April 2020, October 2020-April 2021	Pneumology
196	9	May 2021, May 2022, September 2022, November 2022, February-June 2023	Maxillofacial Surgery
197	9	January-September 2023	Radiology Day Surgery
198	9	January-September 2023	Orthopaedics Day Surgery

199	8	January-July 2019, January 2020	Day Surgery, Week Surgery, Week Hospital
200	8	October 2020-May 2021	COVID
201	8	January-July 2023, September 2023	Urology Day Surgery
202	7	January-July 2019	Digestive and Interventional Endoscopy Week Hospital
203	7	January-July 2019	Neuro-urology
204	7	October-November 20220, February-March 2021, July 2021, September 2021, February 2022	Infectious Diseases COVID
205	7	September 2022-March 2023	Outpatient Macro area of High-Care Complexity
206	7	January-March 2023, May-July 2023, September 2023	Maxillofacial Surgery Day Surgery
207	7	January May 2023, July-August 2023	Pain Therapy Day Surgery
208	7	April-October 2023	Oncologic and Minimally Invasive General Surgery Day Surgery
209	6	March-April 2020, November-December 2020, June-July 2022	Recovery Room
210	6	June 2022, August-September 2022, November 2022, April 2023, July 2023	Otorhinolaryngology Week Hospital
211	6	March-April 2023, June-August 2023, October 2023	Clinical Research Centre
212	6	March-June 2023, August-September 2023	Hepatic and Kidney Transplant Surgery
213	6	March-August 2023	Obstetrics and Gynaecology Day Surgery
214	5	April 2019, September 2019, April 2020, February 2021, November 2022	Hepatology and Gastroenterology
215	5	June-July 2020, October 2020, November 2021, September 2023	Burns and Reconstructive Plastic Surgery Centre Week Hospital
216	5	June-July 2022, September-November 2022	Wound Care Day Surgery

217	5	July 2022, September-November 2022, February 2023	Epilepsy and Parkinson's Surgery
218	5	March 2023, June-July 2023, September-October 2023	Neurosurgery
219	4	May 2019, October-November 2019, July 2023	Ophthalmology
220	4	January-February 2022, April 2022, May 2023	COVID Neurosurgery
221	3	November 2020-January 2021	COVID
222	3	May 2022, October-November 2022	Cardiology
223	3	March 2023, May-June 2023	Neurology
224	2	November-December 2020	COVID Internal Medicine – Former Orthopaedics
225	2	March 2021, July 2021	COVID
226	2	May 2021, June 2022	Maxillofacial Surgery
227	2	January-February 2022	COVID Oncologic and General Surgery
228	2	January-February 2022	COVID Burns and Plastic Surgery
229	2	January-February 2022	COVID Haematology
230	2	January 2022, November 2022	Internal Medicine
231	2	January-February 2022	COVID Gynaecology Day Hospital
232	2	January-February 2022	Subacute Care
233	2	November 2022, October 2023	Digestive and Interventional Endoscopy Week Hospital
234	2	February-March 2023	Cardiology Day Surgery
235	2	September-October 2023	Internal Medicine - Geriatrics
236	2	September-October 2023	Internal Medicine - Geriatrics
237	1	October 2021	Geriatric Rehabilitation Medicine and Neurorehabilitation

238	1	November 2021	Dietetics and Clinical Nutrition
239	1	December 2021	Cardiology
240	1	January 2022	COVID General and Transplant Surgery
241	1	January 2022	COVID Vascular Surgery
242	1	January 2022	COVID Urology
243	1	January 2022	COVID Oncology
244	1	August 2022	Clinical Research Centre
245	1	October 2022	Clinical Research Centre
246	1	November 2022	Radiology Week Surgery
247	1	December 2022	Cardiology
248	1	February 2023	Outpatient Macro area of High-Care Complexity
249	1	October 2023	Oncologic and Minimally Invasive General Surgery Week Surgery
250	1	October 2023	Digestive and Interventional Endoscopy Day Surgery
251	1	October 2023	Radiology Day Surgery
252	1	October 2023	Thoracic Surgery Day Surgery

9. Acknowledgments

I would like to express my deepest gratitude to Professor Lorenzo Giovanni Mantovani for his invaluable guidance, support, and mentorship throughout my PhD journey. His expertise and insightful advice have been instrumental in shaping both my academic and professional growth. I am sincerely thankful to Dr. Sara Conti for her encouragement, thoughtful supervision, and for being available to provide constructive feedback and direction. I would also like to thank all the members and colleagues of the Centro di studio e di Ricerca sulla Sanità Pubblica (CESP) who taught me valuable things during my PhD as well as Manuel, Lisa, Cristina e Isabella who shared this journey with me.

I would also like to extend my heartfelt thanks to Dr. Tjibbe Donker for his guidance, for sharing his expertise, and for offering a broader perspective that has enriched my understanding and contributed significantly to my development as a researcher.

It has been a privilege to learn from and work with such dedicated and inspiring mentors. It is precisely thanks to them that, under my supervisors' guidance, I had the opportunity to publish papers sharing the results of my researches during PhD with the scientific community. Part of this thesis, the section concerning the German hospital, has in fact been published in August 2025 in the Journal of Hospital Infection, Volume 162, pages 68–75. It is my hope that the remaining part may also be published, in order to give greater resonance to the work within the scientific community to help public health regulators designing new strategies against the spread of ARB.

Furthermore, I would like to thank my parents, Maria Pia and Dino, for always being my greatest supporters and for their love and teachings. A big thank you also goes to Carlo, my special partner, who loved me and supported me throughout this entire journey and with the

thesis. Another thank you goes to old friends and among them to my friend Federico, whom I've known since the early years of university, and whose advice, luckily, was not followed.

I would also like to thank some people I met during this PhD: my friends of Tiramisù - Alba, Fede, and Marti –; Fransisco; Giuliano; Francesca; Shyam, Leo, Tatz, Fra, Simo and our 11-floor kitchen gym side gang; all the wonderful people I met at Residenza U12. Without you, this journey would not have been the same… I would not know how to prepare the most famous Tiramisù in four consistencies, how to build a gingerbread house, how to play EUNO and Saboteur, all the techniques to attend perfectly the *Innovation Pub*, where to find the best pizzerias in Milan and its surroundings, the area of Porta Venezia and its flamingos, how to make a delicious chai, that tour never stops, how to share moments in such a special way. I would also like to thank people living in my new home U42 who are giving me cultural exchanges and nice table tennis games nights: it was hard in the beginning in a new empty place but together is always better.

Another thank you goes to the city of Milan, which hosted me, offered countless opportunities to discover new things, and, together with my three colleagues, gave me the chance to present our group contribution at La Biennale di Venezia Architettura 2025.

Finally, my deepest gratitude goes to the University of Milano-Bicocca which, despite all the energy that the research and PhD required, offered me amazing initiatives and countless opportunities to grow in many different fields. Here, and in Milan, I truly felt at home. And as we can admire engraved on the magnificent sculpture in front of U6 by Pomodoro, an artist from my own homeland: "Lo sai: debbo riperderti e non posso".